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NEW HEALTH CARE TECHNOLOGY AND THE CANADIAN HEALTH CARE SYSTEM: A CRITICAL ANALYSIS OF THE INTRODUCTION OF EXTRACORPOREAL SHOCK WAVE LITHOTRIPSY INTO THE PROVINCE OF ALBERTA

by

LAWRENCE C. WISER

A THESIS

SUBMITTED TO THE FACULTY OF GRADUATE STUDIES
AND RESEARCH IN PARTIAL FULFILMENT OF THE REQUIREMENTS
FOR THE DEGREE OF MASTER OF HEALTH SERVICES ADMINISTRATION

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AND COMMUNITY MEDICINE

EDMONTON, ALBERTA

FALL, 1989

THE UNIVERSITY OF ALBERTA

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THE UNIVERSITY OF ALBERTA

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The undersigned certify that they have read, and recommend to the Faculty of Graduate Studies and Research, for acceptance, a thesis entitled NEW HEALTH CARE TECHNOLOGY AND THE CANADIAN HEALTH CARE SYSTEM: A CRITICAL ANALYSIS OF THE INTRODUCTION OF EXTRACORPOREAL SHOCK WAVE LITHOTRIPSY INTO THE PROVINCE OF ALBERTA, submitted by LAWRENCE C. WISER in partial fulfilment of the requirements for the degree of Master of Health Services Administration.

(PHD)
Supervisor

Ian [illegible] MD PhD

Philip Jacobs

Date: 10.5.89

DEDICATION

To my family whose love and support has been steadfast through the good times and the bad.

ABSTRACT

The rapid proliferation of new health care technology with its associated expense may be the greatest threat to Canadian Medicare since its inception. In every province of Canada, health care budgets strain under the weight of increased costs of new methods of treatment, most of which have been implemented and diffused into the health care systems of each Province without scientific proof that these treatments will yield a positive effect on patient health status.

The purpose of this thesis is to look at the present mechanism of assessing and approving new "embodied" health care technologies as they arrive on the scene in Canada. This is done utilizing the new treatment modality of Extracorporeal Shock Wave Lithotripsy (ESWL) in the treatment of urolithiasis (kidney stones) as an example.

The topic is introduced in Chapter I. Chapter II looks at the methodological issues involved in a full evaluation of a new technology. Chapter III follows the historical development of different treatment modalities for urolithiasis through the ages up to, and including the appearance of ESWL. Chapter IV describes the testing of ESWL and results of its first use in humans, culminating in the diffusion of the technology throughout North America. Chapter V outlines the negative side effects (bioeffects) of treatment with ESWL.

Chapter VI looks sequentially at the mechanisms in place presently in the United States, Canada and Alberta to ensure that new technology is implemented safely into each system. Chapter VII presents methodology for the economic analysis of ESWL under the appropriate circumstances. Chapter VIII is the final chapter of the thesis and holds the conclusions of the presentation and offers eight (8) recommendations for making the system safer as more recent medical technology attempts to enter the Canadian health care system.

The recommendations and conclusions of Chapter VIII take the reader "full circle," and he/she is left waiting, with some reservations, for the next technological "miracle" to appear.

It is believed that there is a lesson to be learned from reading this thesis. That lesson is that if action is not taken regarding new medical technology entering the system, and taken very soon, Canada's most popular "social program" may disappear, or be so altered as to be unrecognizable compared to what Canadians cherish and take great pride in today.

ACKNOWLEDGEMENTS

I would like to acknowledge and thank a number of persons without whose support and acumen this project would have been impossible.

First, Dr. Richard Plain, my thesis supervisor, who over the two years of this project became not only a true mentor, but also a friend and confidant.

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from outside of government.

The wisdom provided by Dr. "Mo" Cheung allowed me to extend my insight into this topic. This contribution, along with the provision of other data from the Department of Health Economics and Statistics of Alberta Health proved vital in seeing the overall effect that lithotripsy services will have on resource allocations of Alberta Health.

The contributions of Ms. Lillian MacPherson, head of the John A. Weir Law Library, were vital to the conclusion of this project. Her ability to cut through mountains of legal detail and follow the intricate minuet of changes in statutes and orders-in-council would have been impossible to do without.

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CHAPTER I

INTRODUCTION

As health care resources become even more scarce,[1,2] it is vital that governments ensure that any new health care technology works before implementation and diffusion throughout the Canadian system. This observation has been brought into sharp focus in the province of Alberta with the decision by the provincial Government to purchase, implement, and diffuse the new technology of Extracorporeal Shock Wave Lithotripsy (ESWL) for treatment of urolithiasis and cholelithiasis (kidney stones and gallstones, respectively), while some authors still question whether this technology is of benefit.[3,4] Such action is not unusual in the Canadian health care system, in which "the bulk of the evaluation of technology takes place after the diffusion process."[5] In the case pertaining to ESWL, the Government of Alberta has not acted alone in this instance[6] and the problems are larger than just the actions of one provincial government.[7] The avalanche of support which greeted ESWL was based on "proof" that this method of treatment (at least for kidney stones) was safer[8-10] and more efficient (cost-effective),[11,12] than alternative forms of treatment. Such statements implied that the effect of ESWL on patient health status was known,[13] but before the 83rd Annual Meeting of The American Urological Association in June of 1988, Dr. James E. Lingeman noted during his presentation, the following:

> it should be recognized that the rapid acceptance and adoption of ESWL has been facilitated, in part, by the false perception that this technology is entirely safe and that shock-wave treatment does not induce severe, acute, or chronic side effects. There are now numerous clinical and experimental reports that present evidence that ESWL can cause severe, acute effects.[14]

These words were repeated almost verbatim in a publication two months later.[15]

The fact that there is now some question, as to the efficacy and effectiveness of this new technology in the treatment of urolithiasis is not surprising, given the way that new health care technologies make their appearances in the Canadian health care system. Commenting to that effect, Feeny[16] et al. note:

> New health care technologies have generally been greeted with enthusiasm both by health care providers and the consumers of health care services, who have great faith in their effectiveness. Seldom, however, are new technologies fully evaluated before their widespread implementation. Enthusiasm for a technology frequently wanes as it fails to live up to advertised claims and hoped for benefits.[17]

Purpose of the Thesis

As implementation and diffusion of ESWL is already well established in Canada, the question which this presentation seeks to answer is "What is the mechanism for assessing and approving new 'embodied' health care technologies as they arrive on the scene in Canada?" The purpose of the thesis is to provide an answer to this question.

Scope

The focus of this presentation is on the efficacy and effectiveness of ESWL rather than its efficiency. This stems from the fact that the economics of a medical procedure, process, or technology cannot be determined if it cannot be shown scientifically that the technology is effective. It makes no sense to attempt to prove efficiency of a medical procedure or technology before it has been proven that the technology has the effect of enhancing the health status of those being treated with it.[18]

Limitations

As was mentioned, ESWL is currently being used in the treatment of stones of the kidney and biliary tracts. There is recent evidence showing that it may work in the treatment of cancer.[19,20] Such findings generate a scope far too enormous to be dealt with in one presentation. Therefore, the scope of this presentation will limit itself to the treatment of only urolithiasis by ESWL; specifically lithotripsy given by machines manufactured by Dornier Medical Systems, Inc., and Siemans Medical Systems, Inc. Alternate forms of treatment which preceeded the advent of ESWL (and are still being used with success) will be discussed briefly in the interest of completeness. Following such discussion, the reader will be better able to understand why the technology of ESWL took the profession by storm.

Format of the Thesis

Chapter I of this presentation has introduced the reader to the issue to be examined by this thesis. Chapter II discusses the methodological issues involved in the full evaluation of a new technology. Chapter III looks at the nature of the disease under discussion and its means of treatment, while Chapter IV looks at the means by which the new technology of ESWL was tested and then implemented. Chapter V discusses the most recent literature pertaining to ESWL, which implies that the efficacy and effectiveness of the technology is questionable. Chapter VI examines present mechanisms in place in North America to assure public safety as new technologies are implemented and diffused. Chapter VII provides an explanation of the manner in which an economic analysis of the technology should take place (when it is time for such an analysis). The final chapter, Chapter VIII, offers the author's conclusions and recommendations for making the Canadian system better at assessing new technologies as they appear on the scene.

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2. Lasha Morningstar, "Cut Costs, Minister Warns Alberta Physicians and Patients," Canadian Medical Association Journal 135 (15 November 1986): 1180-85.

3. Sabri Challah and Nicholas B. Mays, "The Randomized Controlled Trial in the Evolution of New Technology: A Case Study," British Medical Journal 292 (29 March 1986): 877-79.

4. Albert G. Mulley, Jr., Karen J. Carlson and Stephen P. Dretler, "Extracorporeal Shock-Wave Lithotripsy: Slam Bang Effects, Silent Side Effects," American Journal of Roentgenology 150 (February 1988): 316-18.

5. David Feeny, Gordon Guyatt and Peter Tugwell, eds., Health Care Technology: Effectiveness, Efficiency and Public Policy (Montreal: The Institute for Research on Public Policy, 1986), p.10.

6. Douglas C. Perry, M.D. (Vice-President Medical, Misericordia Hospital), "Summary of Site Visits," File of the Vice-President Medical, Misericordia Hospital, Edmonton, 20-22 April 1988. This summary is an account of the observations made by physicians on the medical staff of The Misericordia Hospital of a trip which was explicitly designed for them to observe the operations of an ESWL unit first hand. The cities visited were: Winnipeg (Winnipeg Health Sciences Center), Salt Lake City (two site visits: University of Utah Health Sciences Center and The L.D.S. Hospital) and Vancouver (Vancouver General Hospital). Clearly ESWL was already a part of the North American health care system prior to these Alberta visits.

7. The Honourable Perrin Beatty (Minister of National Health and Welfare) to Lawrence C. Wiser, 29 March 1989, Appendix B to this thesis.

8. Christian Chaussy and Egbert Schmiedt," Shock Wave Treatment for Stones in the Upper Urinary Tract," Urologic Clinics of North America 10 No. 4 (November 1983): 743-50.

9. United States Department of Health and Human Services: National Center for Health Services Research and Health Care Technology Assessment, *Summary of Safety and Effectiveness Data: Dornier Lithotripter, Model HM3* (Rockville, Maryland: U.S. Public Health Service, 1985), p.18.

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11. James E. Lingeman et al., "Cost Analysis of Extracorporeal Shock Wave Lithotripsy Relative to Other Surgical and Nonsurgical Treatment Alternatives for Urolithiasis," *Medical Care* 24 No. 12 (December 1986): 1151-60.

12. Louis J. Aronne et al., "Cost Analysis of Extracorporeal Shock-Wave Lithotripsy," *Urology* 31 (March 1988): 225-30.

13. Michael F. Drummond, Greg L. Stoddart and George W. Torrance, *Methods for the Economic Evaluation of Health Care Programs* (Toronto: Oxford University Press, 1987), pp. 5-7.

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19. Gosse O. N. Oosterhof et al., "The Cytotoxic Effect of Vinblastin on the Dunning PAT-2 Prostate Cancer is Potentiated by In Vivo and In Vitro Exposure to Electromagnetically Generated Shock Waves (Siemans, Lithostar)," *The Journal of Urology* 141 No. 4, Part 2 (April 1989): 226A, abstract 228.

20. Jan Willem van Dongen et al., "The Energy of High Energy Shock Waves on Human Prostatic Tumor Cells," The Journal of Urology 141 No. 4, Part 2 (April 1989): 512A, abstract 1387.

CHAPTER II

THE METHODOLOGICAL ISSUES IN THE FULL EVALUATION OF A TECHNOLOGY

Sackett[1] and Drummond[2] et al. have demonstrated a method for assessing any new health care technology. These authors propose three questions which must be answered prior to the implementation and diffusion of any new technology into a health care system:

(1) Has it been proven to be efficacious (Can it work)?

(2) Has it been proven to be effective (Does it work)?

Only when these two questions have been answered affirmatively is there any value in proceeding with an economic analysis, which answers the question of:

(3) How efficient will it prove to be (What is the least costly method of making it work)?

Answering the first question (efficacy) is generally not the most difficult of the three. The answer generally involves more physical, chemical, and/or engineering expertise in finding its solution.[4]

Answering the second question (effectiveness) is a different matter entirely. Clinical expertise at this point, in the form of a randomized clinical trial (RCT),[5] is the primary tool in this assessment. For it is this step that answers another critical question: "Does this form of treatment (technology) improve patient health status?" Only by the incorporation of randomization in the research methodology of a clinical trial, can anything be said concerning causality.[6-9] Guyatt et al. point out, that only by randomization can extraneous variables affecting outcome of the study be balanced.[10] This is because in randomization of patients to different treatment groups, "not only are known prognostic factors likely to be distributed equally between the two groups, but those factors that influence outcome but that we do not know about, or cannot measure, will have a similarly even distribution."[11] Therefore, these authors conclude, "trials in which patients are allocated according to a randomization schedule - randomized control trials - provide the most valid assessment of the technology's effectiveness."[12]

Despite these facts, the medical profession[13] and governments remain incorrigible with respect to recognizing the necessity of establishing effectiveness via the use of an RCT prior to approving the use of a procedure or service.[14] Nowhere in the literature was this better illustrated than in the ongoing debate, lasting three months, which occurred in the British Medical Journal in 1986 concerning whether a randomized clinical trial, which would look at ESWL in Britain, was necessary. The debate was fueled by the British Department of Health and Social Security's (DHSS) decision to initiate an RCT and their later decision (because of pressure brought to bear by the medical "Establishment") to recant that decision.[15]

The debate began with an explanation by Challah and Mays[16] of the reasons why an RCT of ESWL was necessary and the statement (in light of the DHSS decision not to proceed with such a study) by these authors that:

> There appear to be two standards for innovations in medicine: one which demands rigorous assessment of new drugs by proper trials; and a second which allows the introduction of expensive technology and new techniques on the strength of descriptive reports.[17]

In support of their claim that an RCT was necessary, and evidence of where lack of such a study could lead, Challah and Mays pointed to outdated medical treatments. Such treatments as gastric freezing, high concentration oxygen for neonates (which can cause blindness by the process of retrolental fibroplasia[18]), and insulin coma in the treatment of schizophrenic patients, were treatments introduced without benefit of an RCT and "subsequently abandoned because they proved ineffective or unsafe."[19]

Rebuttal of this position was swift as Dudley[20] commented:

> We might ask them (Challah and Mays) if they would care to have an operation performed on themselves using the kitchen as the operating environment, a dirty knife wielded by a gentleman in a filthy frock coat as the instrument, and without benefit of anesthesia - because neither antisepsis nor anesthesia has been subject to clinical trial.[21]

A rebuttal of Dudley's position was offered by Hensley[22] two weeks later who noted, in commenting about the proper use of medical technology already implemented (specifically the use of penicillin, asepsis, and appendicectomy) and diffused without RCT, that "In view of the efficacy of these manoeuvres a relatively small clinical trial would have produced an early and dramatic result."[23] Guyatt et al. list such special circumstances in which a new technology may be safely implemented and diffused without RCT being necessary.[24] These circumstances are very rare. Wickham[25] attacked Challah and Mays by stating "Had they personally managed over 3,000 cases of renal stone disease in a 20-year period they might be better placed to evaluate the quantum advance in the treatment of renal stones represented by the advent of extracorporeal shock wave lithotripsy."[26] The misconceptions, shortcomings, and problems involved with the intuitive approach to problem solving, as demonstrated by Wickham, have been well chronicled by Tversky and Kahneman[27] as well as other authors.[28]

I. **Modern Examples of the Need for RCTs**

The examples given by Challah and Mays[29] of medical therapies gone awry because of the lack of RCTs, are actually fairly ancient examples. More recent examples (later rectified by RCTs) include: the use of intermittent positive pressure breathing (IPPB) as prophylaxis against post-operative respiratory complications,[30,31] and the use of the drug hydralazine in the treatment of congestive heart failure.[32,33]

Of particular interest to this presentation is a technology (also developed by the Germans) whose course of assessment parallels the course of ESWL but which was not implemented because an RCT showed no significant positive effect on patient health status. That technology is "endoscopic laser photocoagulation," which has been used in the treatment of actively bleeding peptic ulcers. It was initially described very positively by German investigators[34] and British researchers[35] who initially found it "a safe and effective hemostatic method"[36] (the term "safe and effective" has been used repeatedly in the descriptive case studies relating to ESWL). Later studies[37] of this technology, however, found "there were no statistically significant differences between the laser and control groups in any prognostic category, with regard to immediate or long-term hemostasis, the need for surgical intervention, or death in the hospital."[38] On the basis of the results of this RCT, this expensive technology was not implemented, resources were freed to be channeled elsewhere, and most people were satisfied.[39]

Table 1 (see following page) is a summary table of all those medical treatments that were at one time very much "in fashion" for the treatment of assorted different medical pathologies, but later were abandoned when it was demonstrated they had no positive effect on the health status of a patient with that particular illness and, in fact, caused harm to some patients.

TABLE 1

Summary Table of Medical Treatments Brought into the Health Care System and Thought to be Effective, but later Abandoned Because of Ineffectiveness,

1. Gastric freezing for bleeding peptic ulcer.[14]
2. Inhalation of oxygen by neonates - later found to cause permanent blindness by retrolental fibroplasia.[14]
3. Insulin coma (hypoglycemia) for the treatment of schizophrenia - resulting in permanent brain damage if serum blood sugar became too low.[14]
4. Intermittent Positive Pressure Breathing (IPPB) as prophylaxis against postoperative respiratory complications.[31]
5. Use of the drug hydralazine in the treatment of congestive heart failure.[33]
6. Endoscopic Laser Photocoagulation for the treatment of bleeding peptic ulcer.[37]

Resistance to the assessment of new medical technology by RCT before implementation and diffusion is gradually fading. Examples of this can be found in statements such as that by Dawson,[40] who in paraphrasing ethicist Michael Lockwood, says of RCTs, "Any new treatment should be subjected to the rigors of a proper clinical trial before it has a chance to become so entrenched that the profession is likely to judge that any such trial is unethical."[41] This statement may explain why, in the case of ESWL, an RCT has not been done.

New examples of RCTs are becoming very prevalent in the medical literature of today. They have shown in Montreal that some forms of elective outpatient surgery, while cost efficient at the organizational level, are cost inefficient at the societal level.[42] RCTs have recently demonstrated the effectiveness of drugs in treating serious kidney conditions[43] and atherosclerotic coronary heart disease as well.[44] Might it possibly be hoped that the RCT will become the "gold standard" used by both government and the profession in the assessment of new medical technologies?

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2. Michael F. Drummond, Greg L. Stoddart and George W. Torrance, *Methods for the Economic Evaluation of Health Care Programmes* (Toronto: Oxford University Press, 1987), pp.5-17.

3. Ibid., pp.7-17.

4. United States Department of Health and Human Services: National Center for Health Services Research and Health Care Technology Assessment, *Summary of Safety and Effectiveness Data: Dornier Lithotripter, Model HM3* (Rockville, Maryland: U.S. Public Health Service, 1985), pp. 8-9. These pages (encompassing Section VI(A)), which are entitled "Laboratory and Animal Testing," describe prototype testing of the Dornier Model HM1 Lithotripter. Such testing included physical and laboratory bench testing along with *in vitro* tests of tissue cultures.

5. Gordon Guyatt et al., "Guidelines for Health Technology Assessment: Therapeutic Technologies," in *Health Care Technology: Effectiveness, Efficiency and Public Policy*, ed. David Feeny, Gordon Guyatt and Peter Tugwell (Montreal: The Institute for Research on Public Policy, 1986), pp.57-77.

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7. Laurna Rubinson and James J. Neutens, *Research Techniques for the Health Sciences* (New York: Macmillan Publishing Co.,1987), pp. 316-17.

8. Donald T. Campbell and Julian C. Stanley, *Experimental and Quasi-Experimental Designs for Research* (Boston, Mass.: Houghton Mifflin Company, 1966), pp. 22-26. The authors point out the necessity of randomization for true experimental designs as they discuss Tests of Significance for their classification of Experimental Designs 4-6.

9. Michael Enzle, Ph.D., professor of Social Psychology and chief instructor for Psychology 441, a course which was taken by the author from September to December 1988 and

which stressed the importance of true experimental design in establishing causality. Of particular concern in this class were a number of exercises to point out the inadequacies of strictly correlational data in the establishment of causality. This class was offered by the Department of Psychology, University of Alberta, Edmonton.

10. Op. cit. 5 above, p. 63.

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13. David H. Spodick to the editor, British Medical Journal 292 (17 May 1986): 1333-34.

14. S. Challah and N. B. Mays, "The Randomized Controlled Trial in the Evaluation of New Technology: a Case Study," British Medical Journal 292 (29 March 1986): 877-79.

15. Ibid.

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CHAPTER III

THE NATURE OF THE DISEASE AND ITS MEANS OF TREATMENT

I. Historical Overview

The history of the treatment of urolithiasis dates well back into the antiquity of mankind. Clearly stated in the Oath of Hippocrates[1] is the statement "I will not use the knife even on sufferers from stone."[2] This is an interesting statement (referring to bladder stones) taught by a man who has been described[3] as "a respected physician and an aggressive surgeon."[4] The hesitancy of Hippocrates becomes more clear in the writings of Celsus, a celebrated Roman bladder stone surgeon, whose graphic description of "surgical" entry into the bladder and recommendations for "postoperative" recovery end with instructions which leave the patient's legs "bound together" and the patient himself "in the hands of the Lord."[5] Modern day estimates of a mortality rate (in ancient times) for this procedure of 50%, give good evidence for Hippocrates' instructions to his students to leave kidney stones alone.[6] Hippocrates, however, advocated a flank approach[7] for drainage if either kidney went on to abscess formation.[8]

The development of surgery for kidney stones was very slow because of the very high morbidity and mortality rates. The early physician, Galen, is said to have mentioned kidney stones[9] only to state that he felt that surgical extraction was not "safe or feasible."[10] Cardan of Milan describes the removal of 18 renal stones while draining a renal abscess[11] in 1501, and Hevin[12] is credited as being the first to use the term "nephrolithotomy" in 1775. In Paris, Civiale, in 1824, passed a stiff metal tubular device (lithotrite) up the urethra of a living patient in order to crush bladder stones blindly.[13] In 1872, Ingalls performed what is thought to be the first "deliberately planned nephrolithotomy" at Boston City Hospital.[14] In 1898, the English surgeon Morris reported the results of surgery done on "healthy" kidneys in 34 patients undergoing nephrolithotomy for removal of stone. This surgery was performed before the kidney had reduced itself to a mere abscess sack.[15] Morris reported only one death in this series. At last it appeared that the forebodings of Galen were dispelled, and the modern era of surgical treatment for urolithiasis had begun.

II. Surgical Treatment

Open surgical removal of kidney stones was the most common form of treatment for this pathology until the introduction of percutaneous nephrostolithotomy[16] (PCNL) in 1976 and the emergence and rapid rise in the popularity of ESWL[17,18] in the 1980s. Both of these more recent treatments for urolithiasis will be discussed shortly in this presentation.

Open surgery for kidney stones, as Hippocrates warned, is not without risks. This fact has been pointed out by the United States Office of Health Technology Assessment[19] (OHTA).

"The use of open surgery carries the risks of bleeding, infection, persistent urinary draining and urinoma, as well as the risk of a loss of the kidney after multiple surgeries."[20] The preceeding list is not all-inclusive regarding the morbidity of stone surgery. Addressing the question of postsurgical hypertension (high blood pressure) following surgery for stone removal, Boyce and Elkins[21] reviewed 100 cases of extensive surgery for stone removal and found that only two patients became mildly hypertensive post-operatively, neither patient requiring medication for control of the hypertension.[22]

Similarly, only two of these 100 patients demonstrated a progressive reduction of renal function postoperatively. The work of these authors was confirmed four years later in another study by Stubbs[23] et al. However, a recent paper by Schulze[24] et al. presents data which is in conflict with these two studies and suggests there may be a postoperative deterioration of renal function following open surgery for urolithiasis.

Postoperative hypertension, as well as deterioration of renal function are germane to a discussion of ESWL because as will be shortly demonstrated, the former condition (hypertension) is a genuine problem in the post-ESWL data to date,[25,26] and there are still many unanswered questions regarding the latter.[27,28]

Boyce[29] presents data encompassing 1,065 renal operations for removal of renal calculi over a twenty-year period (1963 - 1983) at Bowman Gray School of Medicine at Wake Forest University. The median patient age was 44.6 years and the mortality rate within three months following the procedure was 0.38%. This corresponds markedly to a study done by Gonzalez-Serva, Weinerth and Glenn,[30] as well as that of Sakatti and Marshall.[31] Both of the latter groups took a wide-ranging look at all forms of renal surgery which included (but was not specific for) surgeries relating to the removal of renal calculi. These studies included other, non-stone related conditions as well. Gonzalez-Serva et al. studied a group of 814 renal procedures and found a mortality rate[32] of 1.35%. Sakatti and Marshall studied 12,470 "urological operations" and found the mortality rate[33] to be 1.5%.

The best data available presently[34] indicates a mortality rate of 0.38% for surgical treatment of urolithiasis,[35] with a hospital stay[36] averaging 7 to 10 days duration, and an absence from the job of 4 to 6 weeks.[37]

This is comparable to a mortality rate for the elective removal of a gallbladder (cholecystectomy) because of gallstones, varying between 0.1%[38] and 0.5 %,[39] with an average hospital stay comparable to the surgical treatment of urolithiasis.[40]

III. Percutaneous Nephrostolithotomy and Its Associated Procedures

As was discussed in the preceeding section, surgery was basically the only effective treatment for urolithiasis since mankind became intelligent enough to care about such things. The treatment of renal stone disease changed forever with the report (by Fernstrom and Johansson[41]) of a technology for removing kidney stones called percutaneous nephrostolithotomy (PCNL). This technique was less invasive, offered lowered morbidity and mortality rates, was more effective (requiring fewer days in hospital per treated stone), and enabled the stone sufferer to return to full activities much quicker than blunt open surgery. By the early 1980s, and before the widespread appearance of ESWL, PCNL was "the treatment of choice" for this condition.[42,43]

PCNL basically involves a controlled "stab in the back" performed usually (but not exclusively) under general anesthesia, and over the affected kidney(ies). An OHTA report[44] elaborates further on the procedure:

> The percutaneous approach involves placement of a needle into the collecting system of the kidney through a small puncture wound in the flank. This is performed using either ultrasound or x-ray for guidance. After it is ascertained that the needle is in the collecting system by the return of urine through the needle, a guidewire is placed into the collecting system through the needle. The needle is removed with the guidewire left in place. A series of catheters with increasingly large diameters or a dilating balloon are placed over the guidewire in order to dilate the tract from the skin into the renal collecting system. Once a large diameter tract has been established, surgical instruments are then

> introduced and the stone can be fragmented endoscopically using either electrohydraulic, ultrasonic or mechanical lithotripsy techniques allowing the small fragments to be removed.[45]

The percutaneous approach to the renal collecting system, as described above, has proved to be a very useful approach in treating the largest of the renal calculi, the so-called "staghorn" calculi. In this condition, the stone is so large that it fills up most of the kidney's anatomical collecting system.[46] Approaching a kidney affected by staghorn calculus formation in a percutaneous fashion permits the staghorn to be "shaved" or "debulked" down to a smaller size by various instruments. When the stone has been debulked to an appropriate size, it may then receive ESWL,[47] or be lifted out with no other procedure necessary.

Although ESWL has absorbed more and more of those patients who would have been candidates for PCNL, what has been observed is that the residue of those patients undergoing PCNL have become much more difficult cases to handle.[48] Leroy[49] et al. followed 143 patients treated primarily by PCNL at the Mayo Clinic before and after the acquisition of a lithotripter at that institution. They found that:

> In the initial large series (before ESWL was available) 12.5 percent of the patients required another endoscopic procedure (i.e., repeat PCNL) to complete the stone removal. In the post-ESWL arrival group, 28 patients (20 percent) underwent a second percutaneous procedure and 31 (22 percent) underwent post-percutaneous ESWL, for a total of 42 percent requiring additional procedures.[50]

As far as complications resulting from PCNL, Lang[51] collected 8,595 cases from a multi-institutional mail survey and found a rate for all complications of 10.8%. He found a mortality rate for the procedure of 0.046%. Segura[52] et al. reported a complication rate of 3.2% as well as one death, in 1,000 patients treated at the Mayo Clinic.

The "stone-free" rate for the removal of the offending stone fragments is higher for PCNL than for ESWL.[53-55] Brannen[56] et al. found that "targeted calculi" were removed at a rate of 97% by PCNL compared to 96% for an open surgical procedure. Segura[57] et al. found a success rate of 98.3% in the aforementioned Mayo Clinic study. These researchers also found a mean length of stay in hospital of 5.2 days for PCNL.

There can be little doubt that PCNL was a great advance over centuries-old attempts at stone removal. The full effect this procedure might have had was blunted by the rapid rise in popularity of ESWL.[58] Nevertheless, even with ESWL touted as the predominant mode of treatment,[59-61] PCNL has a place in the treatment of renal calculi. Segura[63] identifies this when he says "General indications for percutaneous lithotripsy include large stone volume (greater than 2.5 to 3.0 cm.), infected stone, cystine stone, obstructive uropathy, massive obesity, children, ESWL failures, miscellaneous and certainty of final result."[63]

IV. The Appearance of ESWL

(i) Development

The story of the development of ESWL, from mere motivation (to develop the technology) to mainstream urological treatment, is an arduous, and some might say "romantic" one. Finlayson and Thomas[64] comment on the developmental story in anecdotal fashion:

> A stimulus for the initiation of the program was the contrecoup damage that occurred in gas-filled satellites, when they were struck by micrometeorites. At a social gathering, a physician, who was the wife of one of the engineers working on the shock wave project, suggested that the shock waves could be used to break up kidney stones. Subsequently the Dornier Company began a collaborative program with the Department of Urology of the Ludwig Maximilions University in the Klinikum Grosshadern under the direction of Professor E. Schmiedt.[65]

The project nearly floundered because of "imaging problems" related to stone visualization. To solve these problems the researchers turned to ultrasonic visualization which (although it solved the problem of the moment) has led to incorrect assumptions and reports by these researchers several years later. These problems will be illustrated shortly in this presentation. Finlayson and Thomas go on to state that a critical moment in the project occurred when "to secure continued funding, it was necessary to demonstrate efficacy."[66] This was done, and reported in 1976 by fractionating human kidney stones in water (using an "in vitro" method) and later showing that the human kidney stones could be fractionated using the same technique after renal calculi had been surgically implanted in dogs.[67] The project continued, and gained momentum.[68,69]

In 1980 the results of the first trials of "in vivo" treatment with human subjects were published[70] which showed very promising results. Research continued and modifications to the lithotripter were made. In 1982 these researchers enthusiastically reported results on a series of 72 patients.[71] At the time of publication, 59 of these patients had returned for follow-up study and it was found that "The method was used successfully in all patients,"[72] and that "no complications have resulted."[73]

In 1983 Chaussy and Schmiedt[74] reported the results of 559 procedures done on 498 patients. The results showed a "stone-free" rate of 90% following treatment. A residual post-ESWL surgical rate of 0.7% was noted in these patients. Renal function studies (utilizing ^{131}I-Hippuran[75]) carried out before and after ESWL showed that these patients "had in no way impaired renal function. On the contrary a slight but significant improvement in renal function to 106 percent and 110 percent after 5 and 18 months, respectively, was observed."[76]

Other than the above-mentioned renal function studies, no mention is made of acute or chronic side effects of treatment using ESWL. These authors would address this topic in a later paper.

In closing the above (1983) paper, the authors promised unspecified cost savings (i.e., cost-effectiveness) if the form of treatment which they had developed (ESWL) was used for the treatment of urolithiasis. There are inferences (by these authors) as well, that any urologists not using ESWL in the treatment of renal calculi, may not be practicing "good medicine"; they speak of "surgically induced 'preinvalidism'"[77] caused by surgical treatment of renal calculi, which according to "conservative estimates leads to chronic hemodialysis in 5 to 8 percent of patients."[78] This statement flatly contradicts the work of Boyce and Elkins[79] who found evidence of deterioration of renal function in only 2% of patients undergoing surgery for urolithiasis in a study published in 1974. Another study by Boyce[80] examined 1,065 renal surgeries for stone removal and does not mention decreases in renal functioning except in preventative terms.

The previously mentioned recent paper, by Schulze[81] et al., suggesting reduced renal function in patients who have undergone multiple open surgeries for kidney stone disease, does offer some support, however, to Chaussy and Schmiedt's position.[82]

Chaussy and Schmiedt[83] do address the question of the side effects of ESWL merely to dismiss them in a study reported in 1984: "It was proved that kidney stones were destroyed with shock waves without any pathological changes in either the kidney or the surrounding tissue."[84] More recent studies (cited in Chapter V of this presentation) have shown that the above statement is open to question.

None of the studies done by Chaussy and Schmiedt to this point utilized random assignment to any of the groups of patients undergoing ESWL.

(ii) How Does It Work?

Lithotripsy consists of a transfer of energy from a machine (lithotripter) to a stone (calculus) that is causing illness.[85,86] This transfer is accomplished by the utilization of extracorporeal (i.e., produced outside of the patient's body) shock waves. The shock wave is a physical phenomenon which differs from other waveforms in that it does not have a negative component (rarefaction) as do other waveforms that are sinusoidal in nature such as the sound wave.[87] Such a characteristic infers that extracorporeal shock waves consist only of compressive forces with relatively rapid (0.5 micro-second) diminuition.[88] They do attain pressures as high as 1,000 bar,[89] one bar equalling one atmosphere of pressure. **Figure 1** shows the features of the shock wave used in lithotripsy compared to those of the sinusoidal sound wave.

Figure 1

Differences in sinusoidal waveform (a sound wave) and shock wave (produced in ESWL treatment). Note the absence of a negative component (rarefaction) in (B)[90].

Figure 1 not available due to copyright restrictions.

(A)
Sound
Wave

(B)
Shock
Wave

The process by which these shock waves were first produced in what are now referred to as "first generation" lithotripters like the Dornier Model HM3 (which features a water tub) is described by Bomanji[91] et al.:

> Shock waves are generated when a mass moves in a certain medium with a velocity higher than the speed of sound for the same medium. An ultra short high tension electrical discharge is passed under water to form an arc between two electrodes. The electrodes are placed at the first focus of a hemi-ellipsoid reflecter. The fluid surrounding the arc path vaporizes to produce a rapidly expanding gas bubble.[92]

Newman,[93] et al. go on to describe the process further:

> The electrical discharge is of extremely short duration (0.5 microseconds) and results in pressures measuring around 1,000 bars at the second focal point. The majority of this energy is within an area 1.5 cm. in diameter. Because human tissue is mostly water (75 per cent), a shock wave generated in the degassed water is not impeded entering or exiting the body. When the shock waves strike an accoustically denser substance (such as a renal stone), energy transfer occurs; and when the tensile strength of the stone is overcome, fracturization occurs.[94]

A concerted effort has been made to differentiate the shock waves produced in ESWL from the naturally occurring waveforms such as sound waves. There are however, similarities. The most obvious is the way each travels through different media (propagation). Both travel through water easily and with a constant velocity. As was pointed out by Newman[95] et al. and others[96] the human body is mostly water. The shock wave carries vastly more energy within itself, however, than the sound wave. This energy is not expended until the shock wave encounters a change in the consistency of the media through which it is propagated (acoustic impedance[97]). As the wave encounters acoustic impedance, its high energy is given off.[98] Great effort is taken in all forms of lithotripsy to see that the calculus to be fractionated is the first area of acoustic impedance that the shock waves find. **Figure 2 and Figure 3** illustrate ESWL treatment by a first generation lithotripter. As each individual shock wave expends its energy within the stone repeatedly (a process known as "spalling"[99]), the tensile strength holding the stone together is overcome and the stone is fractionated. Successful fragmentation of the stone, allowing it to pass out of the body in a spontaneous fashion, is considered by some to have occurred when the parts of the fractionated stone are smaller than 5 mm.[100] A fierce debate is presently underway in the literature as to what constitutes "successful" fractionation.[101,102]

Figure 2

Focusing of Shock Waves
in the Dornier Model HM3 Lithotripter.[103]

Figure 2 not available due to copyright restrictions.

Figure 3

Undergoing Lithotripsy with the Dornier Model HM3.

Figure 3 not available due to copyright restrictions.

The patient is strapped into a chair support and then lowered into the water tub (which is part of the lithotripter). The television screens shown are fluroscopy screens (note the cross-hairs) which assist the physician to position the patient's kidney stone at the focal point of the shock waves.

(iii) The Advent of a Second Generation Lithotripter

Recent developments in the technology of lithotripsy are pushing the Dornier Model HM3 lithotripter towards obsolescence. The "Siemans Lithostar" lithotripter, produced by Siemens Medical Systems, Inc., generates shock waves by using an electromagnetic acoustic source (rather than the spark-gap technology of the Model HM3), and is a "second generation" lithotripter. Saltzman,[104] in describing its means of shock wave production, says of the Lithostar:

> It establishes a magnetic field between two conducting layers composed of a metallic membrane and coil. An electric impulse moves the metallic membrane. The wavefront, produced in the water cylinder is then directed towards the focal point by an acoustic lens.[105]

The water cylinder described by Saltzman is not a tub such as is characteristic of the Model HM3. The Lithostar is "tubless," and the mechanism of shockwave production more closely resembles that of a firearm. **Figure 4** displays these features.

Figure 4

Siemans Lithostar Shockhead[106]

Figure 4 not available due to copyright restrictions.

The Siemans Lithostar is the lithotripter that was independently chosen by both hospitals in Alberta receiving ESWL technology, and hence it is the model that the Misericordia Hospital of Edmonton will be receiving.[107] It is capable of treating both kidney stones and gallstones.[108]

Summation

The history of urolithiasis and the development of a means of treatment for this condition has been examined in this chapter, with emphasis on the newly evolved technology of ESWL. The question that remains to be answered is, "What mechanisms were utilized to prove efficacy, effectiveness, efficiency, and safety of this technology?" This is the question which will be examined in the next two chapters of this presentation.

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70. C. Chaussy, W. Brendel, and E. Schmiedt, "Extracorporeally Induced Destruction of Kidney Stones by Shock Waves," *The Lancet* 2 (13 December 1980): 1265-68.

71. Op. cit. 17 above.

72. Ibid., p. 417, abstract.

73. Ibid.

74. Christian Chaussy and Egbert Schmiedt, "Shock Wave Treatment for Stones in the Upper Urinary Tract," *Urologic Clinics of North America* 10 No. 4 (November 1983): 743-50.

75. Peter J. Ell and Edward S. Williams, *Nuclear Medicine: An Introductory Text* (Boston: Blackwell Scientific Publications, 1981), pp. 122-28. These pages describe in detail (with diagrams) the essence of how one carries out an ^{131}I-Hippuran "renogram," which is a renal function study of kidney physiology using the radioactive isotope ^{131}I (radioactive-labeled iodine). Two scintillation counters are placed over the kidneys (one over each kidney). The isotope is then injected intravenously. A

healthy kidney will produce a "normal" curve with a rightward skewing effect when "number of scintallations counted" is plotted against "time in minutes." Variations of the curve described above may indicate "Pathology leading to delay in the time activity peak," which includes, "renal artery narrowing, parenchymal damage or dehydration, oliguria, and other conditions compatible with low urinary output."

76. Op. cit. 74 above, p.746.

77. Ibid., p.750.

78. Ibid.

79. Op. cit. 21 above.

80. Op. cit. 29 above.

81. Op. cit. 24 above.

82. Op. cit. 74 above.

83. Christian Chaussy and Egbert Schmiedt, "Extracorporeal Shock Wave Lithotripsy (ESWL) for Kidney Stones. An Alternative to Surgery?" Urologic Radiology 6 (1984): 80-87.

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85. Op. cit. 74 above.

86. Daniel M. Newman et al., "Extracorporeal Shock Wave Lithotripsy," Urologic Clinics of North America 14 No. 2 (February 1987): 63-71.

87. Alan D. Jenkins, "Basic Principles of ESWL," paper presented at the 83rd Annual Meeting of The American Urological Association, Boston, Mass., 3-7 June 1988.

88. Op. cit. 86 above, p.63.

89. Ibid.

90. Op. cit. 61 above, p.38.

91. Op. cit. 28 above.

92. Ibid., p.1284.

93. Op. cit. 86 above.

94. Ibid., p.63.

95. Ibid.

96. Arthur C. Guyton, ed., Textbook on Medical Physiology, 7th ed. (Toronto: W.B. Saunders Co., 1986), p.386.

97. William A. Yost and Donald W. Nielson, Fundamentals of Hearing: An Introduction, 2d ed. (New York: Holt, Rinehart and Winston, 1985), p.16.

98. United States Department of Health and Human Services: National Center for Health Services Research and Health Care Technology, Summary of Safety and Effectiveness Data: Dornier Lithotripter, Model HM3 (Rockville, Maryland: U.S. Public Health Service, 1985), p.3.

99. Op. cit. 19 above, p.5.

100. James E. Lingeman et al., "Extracorporeal Shock Wave Lithotripsy: The Methodist Hospital of Indiana Experience," The Journal of Urology 135 (June 1986): 1134-37. This is what constitutes a "successful" treatment of urolithiasis at this institution. "Clinically insignificant residual fragments," are defined as those fragments which are asymptomatic and less than 5 mm. in diameter.

101. Op. cit. 55 above.

102. J.E.A. Wickham et al., to the editor, British Medical Journal 297 (24 September 1988): 795-96. In this letter the authors make a fervent comment that ESWL should not be considered "successful" unless fragment size is less than 2 mm.

103. Op. cit. 83 above, p. 81.

104. Brian Saltzman, "Second Generation Shock-Wave Lithotripters: Variations, Indications, and Efficacy in the Treatment of Ureteral Calculi," Urologic Clinics of North America 15 No. 3 (August 1988): 385-92.

105. Ibid., p.387.

106. Op. cit. 19 above, p.4.

107. Donald J. Philippon (Assistant Deputy Minister, Hospitals Services Division) to Gerry Hiebert (President, Misericordia Hospital), 12 January 1989, Appendix C to this thesis.

108. Thomas Scharfe et al., "5000 Patients Experience with the Second Generation Extracorporeal Shock Wave Lithotripsy Using the 'Lithostar,'" The Journal of Urology 139 No. 4, Part 2 (April 1988): 226A, abstract 256.

CHAPTER IV

TESTING THE NEW TECHNOLOGY

Chapter I introduced the reader to the problem to be discussed in this thesis; the failure of society to follow proper methodology when implementing a new method of treatment into the health care system. Chapter II presented a model for the proper introduction of new technology into the system. Chapter III looked at the nature of the illness (urolithiasis) that has been chosen for study in this thesis as well as a chronology of the changes in the means of its treatment through time. It looked also at the physical principles behind ESWL and how this method of treatment operates.

Chapter IV will look at how the technology of ESWL was first developed and tested. As the chapter progresses, the implementation of the technology into the various health care systems of the world will be studied with particular emphasis on the introduction of ESWL into North America. Following this, the development of "second generation" lithotripters (e.g. The Siemans Lithostar) and their impact will be studied.

I. Lab and Animal Studies of the Dornier Model

Preliminary tests involving "physical and technical bench tests" were carried out at the Dornier Laboratory in Friedrickshafen, Federal Republic of Germany (F.R.G.).[1] The physical tests looked at such things as: differences in pressure wave relating to differences between the electrode points, varying discharge voltages and discharge rates, and damping and focusing of the shock wave with transmission through tissue.[2,3] These tests showed that it was feasible for shock waves generated extracorporeally to break up human kidney stones. The data provided by these bench studies proved vital in designing the Dornier Model HM3 Lithotripter[4] (the first lithotripter to become commercially available in North America).

In vitro studies were done which looked at and evaluated the rate and energy of stone destruction in kidney stones of differing compositions.[5] The effect of shock waves on blood samples and lymphocyte cultures was also observed.

In vivo studies were conducted on two sets of rats.[6] In the first set all the rats received shock waves and then 50 per cent were sacrificed 24 hours after exposure, the remainder being sacrificed 14 days following exposure. The second set of rats had their thoraces exposed to the focal point of the shock waves, 50 per cent of the rats having no protection, the remainder having their thoraces protected with styrofoam. Each of the "unshielded" rats died of massive pulmonary hemorrhage while all of the "shielded" rats survived and were found (after being sacrificed) to have no cellular abnormalities upon hisologic examination.[7]

It was concluded that the results of both the in vitro and in vivo studies showed "the feasibility of using an extracorporeally generated shock wave to break upper urinary stones without any significant damage to tissue surrounding the kidney."[8] It was noted, however, that "there is a possibility that lung tissues may be severely damaged if exposed to shock waves."[9]

At the same time that the rats were being studied, 35 dogs had human kidney stones surgically implanted in them and were then treated by ESWL. The results of the in vivo dog studies were instrumental in the evolution from Dornier Model HM1 through to Model HM3.[10]

II. Human Studies

It was now felt amongst the researchers that the models of lithotripters under study had demonstrated enough of a margin of safety to allow testing on humans.[11] The human tests were carried out at three individual sites within the F.R.G. and the three different Dornier Models (HM1, HM2, and HM3) were assigned; one to each site.

(i) Testing of the Model HM1 - Dr. C. Chaussy, Munich

The Model HM1 was tested at this site from February, 1980 to May, 1982, and during this time 212 patients were given 236 treatments. The average patient age was 47.4 years for men and 39.5 years for women (with a 2 to 1, male to female ratio).[12]

The criteria for selection to the study were: stone size not larger than 2 cm., absence of any obstruction in the urinary tract, stone visible on X-ray, patient not suffering from other medical disease, and stone not in the ureter.

After some experience with the technique, the criteria were relaxed to allow entry of patients with: partial staghorn calculus, presence of infection in the urinary tract, patients with atherosclerotic heart disease, and stones in the proximal (upper) part of the ureter.[13]

A very standardized protocol of history and physical examinations and lab tests was performed on each patient before undergoing treatment with ESWL.[14] The only unusual examination or treatment was a pre-treatment "^{131}I-Hippuran clearance" study and the fact that each patient had a Foley catheter inserted into their bladder before treatment which was removed two hours following treatment. After treatment, forced diuresis was maintained by intravenous infusion and diuretics for the first twelve hours post-ESWL.[15]

Results of the HM1 study showed that, of the 212 patients treated in this study, 6 (2.8%) required surgery.[16]

Follow-up studies of these patients included X-ray examination at 3 months, renal function studies (types not specified) at 3 and 12 months, and tests of serum creatinine (a very important measure of effective kidney functioning) done at a time 3 months post-ESWL. The final conclusion of the follow-up studies was, "These patients did not experience any clinically significant change in renal function during the follow-up period."[17]

Complications in this study were found to be cardiac "extrasystoles" of the patients' hearts in relation to shock wave release in 18 of the first 23 patients treated. It was this observation which led to the coupling of the lithotripter to the electrocardiographic (ECG) signal of the heart muscle such that the shock wave was released in the "refractory" period of the cardiac cycle, when the QRS complex had reached its peak.[18]

One patient with a very large calculus in the renal pelvis experienced acute urinary retention, became suddenly very anemic, and complained of severe flank pain. A subcapsular hematoma was diagnosed on the third day post-ESWL.[19]

There was one patient death during treatment. A 70-year-old patient with a heart condition underwent cardiac arrest while being lifted from the tub during a change of the tub electrode. This patient did not respond to resuscitative measures. Postmortem examination of this patient showed "acute heart failure of the severely predamaged myocardium, the predamage caused by prior myocardial infarction."[20]

The final statement relating to safety and effectiveness of the Model HM1 at this site was that "the Dornier Lithotripter, Model HM1, was safe and effective for use in the disintegration of upper urinary stones."[21]

(ii) **Testing of the Model HM2 - Dr.s E. Schmiedt and C. Chaussy, Munich**

The Model HM2 began clinical testing at this site in April, 1982, and as the OHTA began their summary report[22] of the Dornier models in August of 1983, the clinical trial was still in progress.

The format for entry into the study and (once admitted) treatment of calculi, was almost identical to that of the HM1 study. By August, 1983, 494 treatments on 425 patients (444 kidneys) had been done utilizing ESWL administered by the Model HM2. Patients' urine was collected and examined (post-ESWL) and showed a 7.4% rate of stone particles larger than 5 mm. Changes in blood and chemistry profiles pre and post-ESWL were found to have "no clinical relevance."[23] The results of this study showed that 32 people (20%) out of the 160 people considered stone-free at discharge required an adjunctive urological procedure (i.e., required another procedure be done to them, such as a cystoscopy).[24]

Seven patients had "anaesthesia-related complications" of which three of these were pulmonary emboli.[25] It was decided of these seven patients, however, that the pathologies considered to be anaesthesia-related, occurred at "a rate no higher than that found in most surgical procedures involving anaesthesia."[26]

Two patients had complications from ESWL treatment that were considered to be ESWL-related. The first was a false-positive diagnosis of renal cyst hemorrhage into the pole of a treated kidney. The second was, once again, a case of subcapsular hematoma of the treated kidney which recovered spontaneously. No further treatment was required for either of these two complications.[27]

The closing statement of the study at this institution noted that:

> the clinical investigation with the Dornier Lithotripter, Model HM2, demonstrated that the device is safe and effective for use in the disintegration of upper urinary stones ... with fewer complications than those reported from percutaneous techniques of upper urinary stone removal.[28]

The preceeding statement (which is included in the OHTA's definitive word about this study) overstates the case. This is pointed out by Lingeman[29] who notes in a 1988 statement comparing ESWL and PCNL:

> The relative merits of ESWL and PCNL may be simply summarized by the concept that ESWL is preferred for simple stone cases with limited stone burden whereas PCNL achieves much higher success rates for virtually all complex stone problems and renal units containing large stone burden.[30]

(iii) **Testing of the Model HM3 - Dr. Eisenberger, Stuttgart**

Testing at this site began on October 14, 1983, and as of May 31, 1984, thirty patients had been treated. No fragments above 5 mm. had yet been noted and "all 30 patients tolerated the treatment well without complications."[31]

In none of the German studies discussed was randomized assignment accomplished to achieve some measure of control of extraneous variables. The implementation of ESWL technology in Germany was done as Challah and Mays[32] had noted, "on the strength of descriptive reports."[33]

III. Implementation and Diffusion of ESWL within North America

As reports of the successful treatment of urolithiasis utilizing ESWL filtered back from Europe, they found an interested audience in the United States.[34] The United States Federal Drug Administration (USFDA) followed the studies being done in Munich and Stuttgart with great interest.[35] With repeated reports in the literature assuring that all the models of lithotripter manufactured by Dornier were "safe and effective," the USFDA proceeded with its own set of human studies.

With an "investigational device exemption (IDE) application number G820906,"[36] the USFDA initiated a large "Cooperative Study" at six major centers spread throughout the country, which treated kidney stone disorders. **Table 2** illustrates the centers involved and their geographic placement.

TABLE 2

Sites, investigators and beginning dates[37]

Table 2 not available due to copyright restrictions.

A standardized protocol of patient selection and treatment was drawn up to be rigorously followed.[38] To be included in the study initially, the patient had to have: only one renal stone, the stone had to be no greater than 2.0 cm. in its diameter, no evidence of infection in the urine, absence of urinary obstruction distal to the stone, normal body habitus with no greater than 30% excess body fat, no major co-existent disease elsewhere in the body, and the patient had to be "Class I or II" in the system of patient classification as outlined by the American Society of Anesthesiologists.[39] This protocol was to be strictly followed until fifty patients had received ESWL treatment in the unit and then the criteria were relaxed such that stones larger than 2 cm., infected stones, and patients with multiple stones could be included.[40]

The report of this study[41] was published in 1986 and its authors include many of the foremost names in Urology in the U.S. (and the world). Data was accumulated on 2,501 treatments in 2,112 patients who met the criteria for inclusion in the study. The patient population was 70% male; 96% of these patients were white, 1.4% black and the remainder of other races.

Results of the study showed that by three months following treatment, 77.4% of the patients with single stones were stone free. Adjunctive surgical procedures such as cystoscopy or ureteral stent placement (a stent being a "catheter-like" device placed in the patient's ureter at the time of cystoscopy and thought to assist a semi-obstructed renal collecting system with drainage into the urinary bladder),[42,43] were required in 9% of these patients before ESWL. Another 8% required adjunctive procedures post-ESWL as well (the main post-ESWL procedures being nephrostomy to relieve secondary renal obstruction or cystoscopy for relief of steinstrassen,[44] i.e., the blockage of the ureter by small stone fragments post-ESWL that become "jammed" in the ureter, usually in the distal one-third of the ureter), for a total of 17%.[45] It was found that 0.6% of the patients of the Cooperative Study went on to require "some type of open incisional operation."[46] Regarding repeat treatments, it was found that 14% of this patient group required two ESWL treatments and 2% required "more than two treatments."

It was found that 7% of the patients suffered from "complications other than urological."[47] **Table 3** shows a compilation of the numbers and percentages of these complications.

TABLE 3

Complications: heart, lungs, anesthesia, other[46]

Table 3 not available due to copyright restrictions.

Two deaths occurred in the 2,112 patients (.095%) studied. These deaths were "related to cerebral vascular accidents (CVAs) and hypertension"[48] and the authors noted,[49] but dismissed, the earlier claim by Kaude[50] et al. suggesting that EWSL may indeed produce hypertension in some of those patients undergoing this form of treatment at their institution (the University of Florida). Such a dismissal by the authors of the Cooperative Study report seems to indicate an unawareness by these authors of a paper published by Charig[51] et al. three months earlier, which reported the deaths of two patients among the 80,000 patients treated worldwide by the Model HM3. A later paper by Sofras[52] et al. did not speak of death related to ESWL, but reported an incidence of cardiac arrest, while undergoing ESWL, of two patients in 2,000 treatments administered by these authors; both patients being found to have "recovered" following resuscitation.

The importance of this U.S. Cooperative Study cannot be overemphasized. It was the results of this study which led the USFDA on December 19th, 1984, to approve the implementation and dissemination of this technology for the first time in North America.[53] At this point, the USFDA were acting upon the recommendations of the OHTA who were on record as saying that:

> The results of the United States investigations at the Indianapolis School of Medicine, Massachusetts General Hospital, and the Baylor College of Medicine, confirmed the results from the European clinical investigations which showed that the Dornier Lithotripter Model HM3, is safe and effective for use in the disintegration of upper urinary stones, i.e. renal calyx stones, renal pelvic stones, and upper ureteral stones.[54]

It should be noted that, at this time, no randomized group assignment had been incorporated into any patient study; either in the U.S.A. or the F.R.G. No physical, bench, or animal studies were performed by the USFDA, which accepted "without question" the studies done by Dornier, the company which produced (and had a vested interest in) this technology.

Perhaps more distressing, is the fact that it appears that the technology of ESWL was given the "go ahead" in North America after experience with only 2,501 treatments in 2,112 patients (the patient population of the Cooperative Study) over a short time span of ten months (February to December of 1984); the time period from first patient treatment in the U.S.A. to USFDA approval of this technology. By definition, such a study can ascertain very little about the possibilities of chronic long-term side effects of a new technology. More frightening, is the ambiguity of the Office of Health Technology Assessment's (OHTA) statement which speaks of approval, and lists only three of the six institutions involved in the study. What about the data from the other sites? **Table 4** (next page) is a table produced from the same page (page 16) of the OHTA's report recommending the approval of ESWL. Three of the six treatment sites are clearly listed as of May 31, 1984. This appears to be the only data which was available at the time which could have led to the above statement by the OHTA (which the USFDA acted upon) regarding safety and efficacy. Could it be, that given the German data, this was the only North American data that was looked at by the USFDA before arriving at their stated conclusions? If this is the case (and it certainly may not be), one has no alternative but to infer that "official" approval was granted to the new technology of ESWL (in the U.S. at least) on the basis of the experience gained in treatment of 327 patients undergoing 365 ESWL treatments in North America.

As evidence continues to mount, that this technology is not as "safe and effective" as it once appeared, approval may have come too quickly. The reasons for this concern will become apparent in Chapter V of this presentation.

TABLE 4

North American Clinical Investigations of the Dornier Model HM3 Conducted as of May 31, 1984[55]

CENTER	INDIANA	BOSTON	HOUSTON
PATIENTS	215	68	44
TREATMENTS			
1	184	17	41
2	28	1	3
3	3	0	0
TOTAL NUMBER OF TREATMENTS	249	69	47
COMPLICATIONS	3	0	0
DEATHS	0	0	0

The above data was all the data that was available when "The Gastroenterology-Urology Devices Panel" met on May 31, 1984 and "recommended that FDA approve the PMA (Pre-Market Approval Application) for the Dornier Lithotripter, Model HM3..."[56]

IV. Testing of the Siemans "Lithostar"

In vitro testing and animal testing of the Siemans Lithostar showed effects on tissues that were not nearly as pronounced as those outlined by Delius[57] et al. in their study of the Dornier HM3. Concerning the Lithostar, the OHTA felt that "These effects were mild to moderate and probably reversible without intervention. These results were supported by previous animal research done, using comparable shock wave technology ..."[58] The "comparable shock wave technology" refers to the studies done in the development of the Dornier Model HM3.

Clinical testing on humans utilizing the Lithostar was done at four institutions in the U.S. (See **Table 5**). Overall, 386 patients were tested utilizing 412 kidneys and 443 treatments.[59] A success rate of 80.6% was noted at discharge following treatment which climbed to 84.7% at follow-up examination three months later.[60] This compares favorably to the 77.4% post-ESWL figure quoted by the Cooperative Study[61] which looked at the HM3 model.

Perhaps more importantly was the fact that 49.5% of these treatments were able to be done without general anesthetic,[62] utilizing instead the analgesic technique of TENS[63,64] (Transcutaneous Electrical Nerve Stimulation). Increases in blood pressure were noted in 4.3% of patients at three-month follow-up examination.[65] This is roughly half the figure noted by Lingeman and Kulb[66] in their examination of patients with calculi treated by the Model HM3. Much more will be said concerning post-ESWL-related hypertension in the following chapter.

TABLE 5

Summary of Safety and Effectiveness Data:
Siemans Lithostar Lithotripter[67]

Institution /Principal Investigators	Number of Patients	Number of Kidneys	Number of Treatments	Average # of Shock Waves per Treatment
Mallinckrodt Institute of Radiology - Drs. McClennan and Clayman	266	282	298	3576
University of Virginia - Dr. Gillenwater	24	27	27	3277
Baylor University, Dallas - Drs. Schnitzer, Frost and Ware	73	78	90	4260
University of Southern California - Drs. Bragin and Boswell	23	25	28	3155
				(Overall Average)
Total	386	412	443	3670

ENDNOTES -- CHAPTER IV

1. United States Department of Health and Human Services: National Center for Health Services Research and Health Care Technology Assessment, Summary of Safety and Effectiveness Data: Dornier Lithotripter, Model HM3 (Rockville, Maryland: U.S. Public Health Service, 1985), p. 8.

2. Ibid., p. 9.

3. C. Chaussy et al., eds., Extracorporeal Shock Wave Lithotripsy: Technical Concept, Experimental Research, and Clinical Application, 2d ed. (New York: Karger, 1986), pp. 21-35.

4. Op. cit. 1 above, p. 9.

5. Ibid.

6. Ibid.

7. Ibid.

8. Ibid.

9. Ibid.

10. Ibid.

11. Ibid., pp. 9-15.

12. Ibid., p. 10.

13. Ibid.

14. Ibid.

15. Ibid.

16. Ibid.

17. Ibid.

18. Ibid., p. 11.

19. Ibid.

20. Ibid.

21. Ibid. This was a conclusion reached by Dornier Medical Systems, Inc., and reported verbatim in the OHTA (Office of Health Technology Assessment) summary of the Model HM3 without comment or challenge.

22. Ibid., p. 12.

23. Ibid.

24. Ibid., p. 13.

25. Ibid., p. 14.

26. Ibid.

27. Ibid.

28. Ibid.

29. James E. Lingeman, "The Role of Lithotripsy and Its Side Effects," paper presented at the 83rd Annual Meeting of The American Urological Association, Boston, Mass., 3-7 June 1988.

30. Ibid., p. 7.

31. Op. cit. 1 above, p. 14.

32. S. Challah and N. B. Mays, "The Randomized Controlled Trial in the Evolution of New Technology: A Case Study," British Medical Journal 292 (29 March 1986): 877-79.

33. Ibid., p. 877.

34. A. G. Mulley, "Shock Wave Lithotripsy: Assessing a Slam-Bang Technology," The New England Journal of Medicine 314 (27 March 1986): 845-47.

35. Op. cit. 1 above.

36. Ibid., p. 15.

37. George W. Drach, et al., "Report of the United States Cooperative Study of Extracorporeal Shock Wave Lithotripsy," The Journal of Urology 135 (June 1986): 1127-33. The table referenced was taken from p.1127 of this publication.

38. Op. cit. 1 above, p.15.

39. Robert D. Dripps, James E. Eckenhoff and Leroy D. Vandam, eds., Introduction to Anaesthesia: The Principles of Safe Practice, 6th ed. (Toronto: W.B. Saunders Co., 1983), pp. 17-18.

40. James E. Lingeman et al., "Extracorporeal Shock Wave Lithotripsy: The Methodist Hospital of Indiana Experience," The Journal of Urology 135 (June 1986): 1134-37. A description of the protocol for this study and the subsequent relaxing of requirements after fifty patients had been treated at a particular site is given on p.1134 of this publication.

41. Op. cit. 37 above.

42. Roy P. Finney, "Double-J and Diversion Stents," Urologic Clinics of North America 9 No. 1 (February 1982): 89-94.

43. Dov Pode et al., "Treatment of Complete Staghorn Calculi by Extracorporeal Shock Wave Lithotripsy Monotherapy with Special Reference to Internal Stenting," The Journal of Urology 140 (August 1988): 210-65.

44. Robert A. Roth and Carl F. Beckmann, "Complications of Extracorporeal Shock-Wave Lithotripsy and Percutaneous Nephrolithotomy," Urologic Clinics of North America 15 No. 2 (May 1988): 155-66. For an excellent description of steinstrassen, the reader is referred to pp. 157-59 of this article under the section entitled "Complications from Passage of Fragments and Particles."

45. Op. cit. 37 above, p. 1127, abstract.

46. Ibid., p. 1129.

47. Ibid.

48. Ibid.

49. Ibid.

50. Juri V. Kaude et al., "Renal Morphology and Function Immediately after Extracorporeal Shock-Wave Lithotripsy," American Journal of Roentgenology 145 (August 1985): 305-13.

51. C. R. Charig et al., "Comparison of Treatment of Renal Calculi by Open Surgery, Percutaneous Nephrolithotomy, and Extracorporeal Shock Wave Lithotripsy," British Medical Journal 292 (29 March 1986): 879-82.

52. F. Sofras et al., "Methodology, Results and Complications in 2000 Extracorporeal Shock Wave Lithotripsy Procedures," British Journal of Urology 61 (January 1988): 9-13.

53. Op. cit. 1 above, p. 16.

54. Ibid., p.18.

55. Ibid.

56. Ibid.

57. Michael Delius et al., "Biological Effects of Shock Waves: Kidney Damage by Shock Waves in Dogs - Dose Dependence," Ultrasound in Medicine and Biology 14 No. 2 (1988): 117-22.

58. United States Department of Health and Human Services: National Center for Health Services Research and Health Care Technology Assessment, Summary of Safety Effectiveness Data: Siemans Lithostar Lithotripter (Rockville, Maryland: U.S. Public Health Service, 1988), pp. 11-12.

59. Ibid., p.12.

60. Ibid., p.15.

61. Op. cit. 37 above, p.1127, abstract.

62. Op. cit. 58 above, p.15.

63. Ronald D. Miller, ed., Anesthesia, 2d ed., 2 (New York: Churchill Livingston, 1986), p.1427.

64. Juan Fernandez et al., "Extracorporeal Shock Wave Lithotripsy Without Anesthesia: a Study Using the Transcutaneous Electric Nerve Stimulator," The Journal of Urology 139 No. 4, Part 2 (April 1988): 325A, abstract 651.

65. Op. cit. 58 above, p.16.

66. James E. Lingeman and Thomas B. Kulb, "Hypertension Following Extracorporeal Shock Wave Lithotripsy," The Journal of Urology 137 No. 4, Part 2 (April 1987): 142A, abstract 154.

67. Op. cit. 58 above, p.13.

CHAPTER V

PROBLEMS AND UNWANTED SIDE EFFECTS

Recently, increasing numbers of publications concerning unwanted side effects (bioeffects) of the treatment of urolithiasis with ESWL have appeared in the literature. At the beginning of this presentation a quote by Lingeman was used to focus the reader on the essence of this presentation as it pertains to lithotripsy. The preceeding material has been presented so that the publications now discussed (which are more recent) can be followed by the reader, and the manner in which ESWL was introduced into North America (of which Canada is a part) may be appreciated. It is worthwhile stating again: "What are the effects of ESWL on patient health status?" Because a randomized clinical trial (RCT) has yet to be effected on this new technology, this question cannot be answered at this juncture.[1]

This chapter will be in different segments and will refer back to material introduced earlier in the presentation.

I. Echoes of Dissension (Rumours of Glory)

In August of 1985 (18 months after the first ESWL treatment in North America) Kaude[2] et al. presented data which was very controversial and disquieting, but retrospectively can only be termed "prophetic." These researchers (from the University of Florida) looked at the acute side effects (bioeffects) of ESWL on the morphology and function of the kidney by using excretory urography (e.g., intravenous pyelography), quantitative radionuclide renography (QRR; i.e., radioisotopic scans of the kidneys), and magnetic resonance imaging (MRI) in 33 consecutive patients undergoing ESWL for renal calculi. (The reader will remember that the University of Florida was one of the six institutions in the Cooperative Study[3].) The results of their study showed the following: (1) excretory urograms demonstrated kidney enlargement in 7 (18%) of 41 treatments, and (2) partial to complete obstruction of the ureter by stone fragments in 15 (37%) of 41 treatments (3) QRR demonstrated a decrease in "Effective Renal Plasma Flow" (ERPF) of more than 5% in 10 (30%) of 33 cases in a kidney which had been treated with ESWL, and (4) partial parenchymal obstruction of the kidney receiving ESWL in 25%, and total parenchymal obstruction in 22% of all the cases of the study. (5) MRI demonstrated the following abnormalities: loss of corticomedullary differentiation, perirenal fluid, subcapsular hematoma, hemorrhage into a renal cyst, and unexplained abnormalities.

These findings were quite unexpected and potentially quite serious (see Section II of this chapter for a discussion of subcapsular hematoma formation of the kidney, sometimes called "Page kidney"[4]). The authors realized the gravity of these findings immediately and stated "we believe that ESWL produces renal contusion similar, if not identical, to that seen in external mechanical trauma (of the kidney)."[5] Of equal concern was "loss of corticomedullary differentiation" demonstrated by MRI involving the renal parenchyma:

> We conclude that the loss of corticomedullary demarcation seen after ESWL is due to the direct effect of ESWL on renal parenchyma and not to hydronephrosis caused by ureteral obstruction. Loss of corticomedullary junction occurs with a variety of renal diseases including glomerulonephritis, acute tubular necrosis, end-stage chronic renal failure, renal artery stenosis and transplant rejection. We believe ESWL should be added to this list.[6]

In closing their paper and in light of their findings, these authors took issue with the statement by Chaussy and Schmiedt[7] made in 1984 that "It was proved that kidney stones were destroyed with shockwaves without any pathologic changes in either the kidney or the surrounding tissue."[8] Addressing this statement directly, Kaude and his associates observe that "this statement was based on an experiment in which 17 dogs with implanted stones were treated with 500 shocks and then sacrificed at 14 days after ESWL."[9] Their statement gained more credibility when Lingeman[10] et al. later pointed out that Chaussy and Schmiedt had used a questionable technique in ultrasound in looking for post-ESWL bioeffects (it had been assumed that more powerful techniques of diagnostic imaging such as CT scanning or MRI had been used in the search for bioeffects rather than the technique of ultrasound). This led Lingeman et al. to say of Chaussy and Schmiedt's data "renal injuries among ESWL patients are considerably more common than the 0.6 value[11] reported by Chaussy and Schmiedt as detected by ultrasound."[12]

Perhaps surprisingly, the paper by Kaude et al. stood alone in its opposition to ESWL for two years. In the interim, many papers again began appearing speaking positively about the new technology[13-15] and praising it as "a primary treatment for urolithiasis whenever applicable."[16]

It was not until a publication by Lingeman and Kulb[17] that concern regarding ESWL was created. These authors reported (retrospectively) an incidence of hypertension of 8.2% amongst 295 of their patients who had been given ESWL for treatment of their stones a minimum of twelve months earlier. Genuine anxiety regarding ESWL now was acknowledged in the urological community.[18] The 8.2% hypertension bioeffect consisted of "new onset hypertension requiring pharmacologic therapy."[19] In addition to those who had received ESWL for their calculi and now required drugs to hold their blood pressure within normal limits, Lingeman and Kulb reported another 15.2% of this post-ESWL patient population who "had an increase in their diastolic blood pressure averaging 16.7 millimeters of mercury, but not requiring pharmacologic therapy."[20] Lingeman and Kulb were at a loss to explain why this was happening. Perhaps more frightening was the discovery that the Cooperative Study (on which so much of the "official" approval by the USFDA had depended) had not looked in more than a routine way at hypertension as a possible complication of ESWL, and not at a post-ESWL distance of twelve months or greater.[21] The Cooperative Study lasted only ten months before approval was granted.

On the same page that Lingeman and Kulb had announced their discovery, there was also a paper by Knapp and Kulb[22] (of the same institution) announcing that, in a parallel study examining 3,620 treatments, they had found an incidence of 0.66% of "subcapsular or perirenal bleeding."[23] More important (and alarming) was the apparent propensity of this form of hemmorhage in patients who were afflicted with hypertension before undergoing ESWL: "the incidence of hematoma in hypertensive patients was 2.5% and 3.8% in patients with unsatisfactory control of hypertension."[24] These authors thus observed a direct effect between perirenal hemorrhage and the level of hypertensive control, in which the incidence of perirenal hematoma was six times greater in poorly controlled hypertensives when compared to the non-hypertensive population undergoing ESWL. One-third of the patients of Knapp and Kulb required blood transfusion.[25] One patient required "selective renal arteriographic embolization" to control hemorrhage.[26] It was also noted that "one patient with bilateral hematomas required short-term hemodialysis."[27]

With the publication of these two papers,[28,29] the technology of ESWL no longer appeared "safe and effective." Perirenal hematoma (i.e., bleeding within and around the kidney), of which "subcapsular" hematoma is the most menacing form, can be a very serious bioeffect of ESWL. The consequences of these hematomas even today are not totally understood.[30] The seriousness of this form of kidney pathology has been known to the medical profession for exactly fifty years. It was first discovered by Page[31,32] who in 1939 published data concerning his work with canine kidneys, and with which the medical profession of today is well aware.[33]

II. The Page Kidney and the "Fibrous Hull"

Early in 1939, Page[34] described a method in which he experimentally produced hypertension in dogs: "It has been found that arterial hypertension can be produced in dogs by wrapping one or both kidneys in Cellophane."[35] Page found that within two to three weeks after his experimental manipulation of the canine kidneys, the dogs developed severe hypertension. Following sacrifice of the dogs, it was found that "the kidney is found to be surrounded by a dense hull of tissue (fibroblastic and collagenous) as much as 4 to 5 mm. thick."[36] In a later publication that same year,[37] Page postulated that the hypertension he had produced in dogs followed the same "physiologic mechanism" as that produced by Goldblatt[38] et al., who had shown in 1934 that constriction of the renal arteries (i.e., renal artery stenosis) produced hypertension.

The clinical significance of Page's findings remained only speculative until the report, by Farrell and Young[39] in 1942, of the case of an 18-year-old boy who at the age of six had been struck in the loin area (an obvious external trauma) with a projectile (a roller skate) thrown by a playmate. The patient now (at the age of 18) was found to be chronically hypertensive with radiologic evidence of renal pathology. The patient's hypertension was cured by removal of the affected kidney (nephrectomy). Postoperative pathologic examination of the removed kidney showed "subcapsular interstitial fibrosis" (i.e., scar formation) of the kidney cortex, and evidence of frank damage of the renal parenchyma: "Several of the glomeruli were replaced by connective tissue. There was some atrophy of the apertaining tubules, associated with interstitial fibrosis and round cell infiltration."[40] The findings in this case were felt by the authors to be very similar to those reported by Page[41,42] in his work with dogs.

More significantly for the people of today, the renal changes described by Farrell and Young are very similar to those described by Kaude[43] et al., and Knapp and Kulb[44], in those patients whose kidneys have been subjected to ESWL. MacKay, Proctor, and Roome[45] reported a case of very severe hypertension ("malignant hypertension") caused by compression of the kidney by a "fibrous hull" of tissue, which had been caused by previous open surgery of the kidney for removal of a renal calculus. The point being made here is not that ESWL is the only thing which can cause formation of a fibrous hull around the kidney, but that when it does form, its consequences can be very severe; even life-threatening.[46]

In 1955, Engel and Page[47] reported the case of a 19-year-old man with severe hypertension caused by a fibrous hull about his kidney. Among their observations concerning this form of hypertension was, "the hypertension did not result from compression of the renal artery, but rather from changes in intrarenal hemodynamics produced by the firm hull surrounding the parenchyma."[48] Again, addressing the damage to the kidney which is correlated with this type of hypertension, they said "The possibility of its development, however, should remind us of the importance of avoiding undue surgical trauma to the kidney and its capsule."[49]

One can only speculate what they would have said about the perirenal hematomas caused by ESWL treatment of renal calculi, but it is doubtful that they would have spoken positively about it.

More recent papers concerning Page kidney include those of Grant[50] et al., who reviewed the experience of the Cleveland Clinic with hypertension related to renal trauma, and that of Sufrin[51] who speaks of modern day therapeutic measures for the Page kidney.

III. Dog Studies Relating to ESWL

As has been noted earlier in this presentation (Chapter IV, Section I), the early investigations involving ESWL and dogs, which were noted by the USFDA,[52] did not report pathological renal damage in the dogs. Similarly, early publications by Chaussy[53] et al. did not speak of such damage. In 1987, Newman[54] et al. Conducted an experiment to detect whether significant morphologic pathology existed in dogs who had been given varying amounts of shock waves to their kidneys in a manner similar to that employed in the ESWL treatment of human renal calculi.

The dogs were divided into two groups, A and B.[55] Group A was to show the immediate effects (48 - 72 hours post-ESWL) of shock waves to the kidney, while Group B was to show the longer term effect (28 - 32 days). The number of shock waves administered varied from 1,600 to 8,000. (It should be noted that the USFDA approved the Dornier Model HM3 Lithotripter for up to 2,000 shock waves for treatment of urolithiasis[56] although there are reports in the literature of up to 5,000 shock waves being used to treat renal stones in humans.[57,58]) Following their exposure to the shock waves, the dogs were sacrificed in order to carry out gross and histologic examination of their kidneys.

The results of this examination showed acute hemorrhage into the renal parenchyma: "Cortical and medullary hemorrhage was noted in all kidneys examined at forty-eight to seventy-two hours."[59] Specifically the authors noted "The predominant histopathologic finding in the renal units examined soon after lithotripsy was damage to thin-walled veins."[60] The observations regarding Group B showed evidence of a scarring process (fibrosis) and were clearly more ominous: "The presence of fibrosis in Group B kidneys is evidence of permanent change."[61]

The observations of Newman et al. were again seen in the work of Delius[62] and Delius[63] et al. who essentially performed the same experiment and delineated parts of the kidney which showed (histologically) areas of damage. This damage was found to consist of: (1) tubular destruction leading to extravasation of blood into the tubuli, (2) diffuse interstitial hemorrhage, (3) venous thrombosis affecting interlobular and arcuate veins, and (4) tubular dilation with hyaline casts. Although damage to the renal vascular tree seemed notably to be on the venous side, these authors noted that "as damage to the arterial wall also occurred we assume, that shockwaves can cause arterial damage and this is the reason for larger hematomas."[64] Such an explanation does seem to be credible in explaining the large hematomas that occur in humans following ESWL.[65,66]

Most recently, the foregoing studies have been repeated by Abrahams, Lipson and Ross[67] and have shown similar results.

IV. Formulating Recent Research into "The Big Picture"

The complete picture regarding the bioeffects of ESWL in the treatment of urolithiasis is still evolving. In a recent paper, Lingeman[68] et al. divide bioeffects into two categories: "Extra Renal Side Effects" and "Potential Renal Side Effects" of ESWL treatment.[69] The latter category is further subdivided into "Acute" and "Chronic" side effects.[70]

In the interests of clarity, it is possible to condense Lingeman et al.'s data down further for the purpose of discussion. This has been done in **Figure 5**.

FIGURE 5

Complications Documented as Occurring with ESWL

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1. Decreased Renal Function (acute and chronic)
   Failure?
2. Perirenal Hematoma (Page Kidney?)
3. Hypertension (Acute and Chronic)
4. Cardiovascular: myocardial infarct
   cerebrovascular accident
5. Death

(i) Decreased Renal Function (Acute and Chronic)

The question of how the shock waves of ESWL affect normal kidney physiology is a good one, which was brought into focus early in 1986 by von Schulthess[71] et al. who examined human kidneys using MRI, after treatment of urolithiasis by ESWL. These authors found that "treated kidneys showed decreased uptake and delayed excretions ... consistent with impaired parenchymal function and urethral obstruction."[72] Also found by their MRI study, were morphologic changes which showed "increases in the size of the treated kidney resulting from edema,"[73] as well as "hydronephrosis of the treated kidney."[74] These were findings, some of which were not described earlier by Kaude[75] et al.

Following the findings of von Schultness et al., Bomanji[76] et al. in a pre and post-ESWL study of 42 patients, used radioactive-labelled technesium scans (a renal function study) which confirmed the findings of von Schulthess et al., but also showed a decrease in renal function of 8% to 21% (mean 16.2%) two to three days post-ESWL in 9 (19%) of these 42 patients.[77] They noted that "Four of these nine patients had returned to pre-ESWL level by three weeks post-treatment."[78] What was noted by these authors, which was not known before, was an increase in the time taken for the radioactive marker to pass through the kidney after it had been treated with ESWL. This was measured as an increase in the "Parenchymal Transit Time Index" (PTTI).[79] The authors felt that "PTTI prolongation may be due either to renal ischemia or to obstruction"[80] in the post-ESWL kidney. Interestingly enough (and possibly a cause for concern), they found two to three days following ESWL a "significant prolongation" of the PTTI of the untreated kidney,[81] for which they conjectured, "A possible explanation could be a reflex autonomic response to renal pelvic stimulation occurring with the fragmentation of the stone by the shock waves."[82] The prolongation of PTTI in both treated and untreated kidneys was felt by these authors to represent a temporary phenomenon as the PTTI of both kidneys "returned to normal by three weeks post-ESWL."[83]

The idea that the decrease seen by Bomanji et al. in renal function was only "temporary" was rejected by Williams[84] et al. who presented data from 91 (61%) of 148 patients treated at the University of Florida. These patients showed chronic decreased renal functioning 17 to 21 months following ESWL for stone disease. The means of detecting this deterioration of kidney physiology was the same as that used by Kaude[85] et al. three years earlier; (QRR). The authors state that "quantitative radionuclide renography disclosed reduced renal function (a decrease in ERPF of more than 5 percentage units) in 10 (30%) of 33 of the treated kidneys..."[86] In this quotation ERPF refers to "Effective Renal Plasma Flow," which is a measure of the amount of blood flowing through the kidneys. Shortly after saying this, the authors make clear the concern with which they view their results:

> we found that 24% of patients had an abnormal decrease in renal function of the treated kidney at 17 - 21 months. The fact that ESWL may result in a significant decrease in the percentage of ERPF to the treated kidney, both acutely and at 17 - 21 months suggests that the decrease in renal function caused by ESWL may be permanent.[87]

In a final comment, the authors speak about the fibrosis (scarring) of the kidney which they have observed accompanying the treatment of renal calculi by ESWL:

> In the immediate post-ESWL period, decreased renal plasma flow may be reasonably attributed to increased interstitial pressure caused by perirenal and intrarenal hemorrhage and the resultant edema. Up to 18 months after ESWL, decreased renal plasma flow may result either from increased interstitial pressure possibly caused by fibrosis due to intrarenal hemorrhage

> or by fibrosis due to the pressure from a perirenal fibrotic process.[88]

The "perirenal fibrotic process" referred to by these authors is the "fibrous hull" referred to by Page.[89,90]

Of particular interest in this instance was Chaussy[91] et al.'s 1984 statement regarding renal function: "We found that one and one-half years after treatment a significant enhancement in function to 110 per cent of the initial performance had been achieved."[92] Addressing this statement in a publication four years later, Lingeman[93] et al. say "Only Chaussy and colleagues reported a significant improvement in renal function one year after ESWL. We were not able to confirm this observation ..."[94]

Also noted as a side effect by Gilbert, Riehle and Vaughan[95] was the loss of protein in the urine (proteinuria) following ESWL to the kidney. These authors reported proteinuria of up to 1.5 grams per 24-hour urine specimen, collected in 26 patients they studied. Such proteinuria is reminiscent of that seen in "Nephrotic Syndrome" (a kidney condition defined by proteinuria of over 3.5 grams per 24-hour urine specimen) which may end in chronic end-stage renal failure and hemodialysis.[96] The authors speculate as to the cause of this post-ESWL-related proteinuria: "Conceivably the measured proteinuria might be the result of excreted hemoglobin occurring with hemolysis, plasma protein in urine resulting from urothelial or endothelial disruption, or altered a

glomerular membrane permeability."[97] It is this last feature (altered glomerular membrane permeability) which is the hallmark of Nephrotic Syndrome.[98] The proteinuria of the patients in this study resolved spontaneously after three months, but then so did the disturbances of renal function (in 3 weeks) noted by Bomanji,[99] et al.

Before leaving the subject of the effect of ESWL produced shock waves on renal physiology, it has been noted during this presentation that much weight was given to pre and post-ESWL renal function studies which showed no significant difference in ^{131} I-Hippuran clearance by the kidney. Such studies were conducted in the evaluation of the Dornier Model HM1 in Munich[100,101] and the Cooperative Study done in the U.S.[102] Results of these "clearance" studies came into question at a recent "Consensus Development Conference" held in Bethesda, Maryland.[103] When asked about the significance of these studies in detecting a decreased "glomerular filtration rate" (the best measure of possible damage to the nephrons of the kidney[104]), Dr. F. L. Coe (Director of Nephrology, University of Chicago School of Medicine) stated: "I would never accept Hippurate clearance as a sole marker for nephron damage. Given the ability of the tubule secretory process to maintain clearance despite reduced glomerular filtration rate, you can underestimate renal injury."[105] If this statement is true, the ^{131} I-Hippuran clearance studies done in most of the early studies relating to the safety of ESWL are highly overrated.

It appears in the initial studies concerning ESWL that too many extraneous factors were in operation. This probability led Dr. K. Carlson of Harvard Medical School to say at this Consensus Conference: "I suggest that we really need a randomized trial of lithotripsy for marginal indications to answer the questions about natural history and long-term complications."[106] In short, what these physicians are saying is that "We really do not know the effect yet of ESWL on patient health status."

(ii) ESWL-Induced Perirenal Hematoma

In their early paper in 1985 which was critical of ESWL treatment for renal stone disease, Kaude[107] et al. noted the incidence of subcapsular hematoma (0.6%) reported by Chaussy and Schmiedt[108] in 1,012 treatments of 896 patients and disagreed with that figure, saying "This incidence is about one-fiftieth the incidence seen in our series, in which hemorrhage, either subcapsular or intracystic, was found in 11 (29%) of 38 treated kidneys."[109]

In a report published in 1987, Baumgartner[110] et al. used MRI to examine 34 patients following ESWL and found 10 (29%) to have either subcapsular hematoma or perinephric fluid. As well, they noted many of the associated findings first described by Kaude et al. in 1985. Summarizing their results, Baumgartner et al. stated: "Our study supports the earlier findings of Kaude et al. indicating morphologic changes in the majority of kidneys after ESWL, although we found a somewhat higher frequency of such changes."[111]

The previously mentioned study of Williams[112] et al. not only looked at renal function studies 17 - 21 months post-ESWL, but also did MRI of the ESWL treated kidneys, leading these authors to state that "MR imaging disclosed evidence of renal trauma (edema or hemorrhage) in 24 (63%) of 38 of these treated kidneys."[113] As the data concerning this bioeffect began to come together, these authors looked at the earlier data of Chaussy and Schmiedt[114] and agreed with Lingeman[115] et al. as they stated in their conclusions:

> Although the originators of the procedure recorded a very low frequency (0.6%) of subcapsular hematoma, a prospective study with MR imaging revealed a much higher frequency (29%) of subcapsular, perirenal and/or intraparenchymal hemorrhage. The difference in the rate of occurrence of renal hemorrhage may be attributed to the much less sensitive sonographic technique used by Chaussy et al.[116]

Continuing discussion of post-ESWL related perirenal hematoma was done by Rubin[117] et al. who looked at a series of 50 post-ESWL patients using computed tomographic (CT) scans and found subcapsular hematoma in 8 (15%), intra-renal hematoma in 2 (4%), and subcapsular fluid collections in 3 (6%). This led to the almost inevitable comparison of their data with that of Chaussy and Schmiedt[118] and Kaude[119] et al. in which they noted that their incidence of 15% for acute subcapsular hematoma, was "much higher than that reported by Chaussy and Schmiedt,"[120] and their data was "similar to the 24% frequency of post-ESWL subcapsular hematoma found on magnetic resonance imaging by Kaude et al."[121]

The paper of Knapp and Kulb[122] which was presented (and referred to already in this presentation) in abstract form in 1987, appeared in definitive form[123] in 1988. There were few changes in this publication which examined 3,620 ESWL treatments in 3,208 patients. The combined incidence of perirenal hematoma following ESWL, if the patient suffered from hypertension already (controlled or uncontrolled), was uniquely high.[124] The appearance of post-ESWL hematoma did not correlate with stone number, size or location, history of stone or renal surgery, malformations of the kidney, patient size and weight, number of shocks used, or energy applied[125] (shockwave number multiplied by the voltage). A valuable observation of these authors, directly relates to the cost effectiveness (or lack thereof) of ESWL:

> The majority of patients (54 per cent) with a perirenal hematoma had a pelvic stone 1 cm. or less in diameter and 64 per cent received 1,000 or fewer shock waves. Interestingly, these patients constitute the group usually considered for outpatient ESWL. We recommend close observation and follow-up within the first 24 hours postoperatively, preferably on an inpatient basis to monitor for post-ESWL complications of perinephric hematoma, ureteral obstruction and sepsis.[126]

With the recommendation by these authors to discontinue ESWL on an outpatient basis, and their observations that some patients (those with hypertension) had a six-fold increase in perirenal hematoma[127] (with all its sequelae) over the incidence quoted by Chaussy and Schmiedt,[128] the benefits of

ESWL were becoming less and less attractive economically speaking.

(iii) Post-ESWL Hypertension: Is there a Causal Relationship?

Much has been said already in this presentation (albeit in a "piecemeal" fashion) about the relationship and discovery of "new onset" hypertension in patients who have undergone treatment of their stones by ESWL. Hypertension is of concern for a whole host of reasons, but mainly because it increases the incidence of atherosclerotic heart disease[129] resulting in myocardial infarction (heart attack) as well as cerebral vascular accident[130] (CVA), commonly known as "stroke." Perhaps the worst problem related to hypertension is that it shortens lifespan (i.e., increases mortality) and productive working life (i.e., increases morbidity). A chronological presentation of ESWL-related hypertension is now offered.

The first paper to critique ESWL and suggest that all was not well was the paper by Kaude[131] et al. which one doing research into ESWL notes referenced time and time again. Although these authors do not state that "ESWL causes hypertension," it is virtually impossible for anyone who is knowledgeable in matters pertaining to Nephrology (the specialty within which the treatment of the condition of hypertension falls) not to catch this implication.

The authors of the Cooperative Study were cognizant of this implication when they referred to Kaude et al's. paper and said "The ESWL procedure has been suggested to cause hypertension but no data in our study tested for this result,"[132] and therein lies a major problem with the approval and implementation of this technology.

It is scarce wonder that Lingeman et al. (who have the largest series of ESWL treated patients in the U.S.) who were cognizant of this fact, kept a diligent lookout for this bioeffect and reported it later.[133] Their report of 8.2% (for the incidence of post-ESWL-related hypertension using the Dornier Model HM3) is very close to that reported by Williams et al. of 8.0%. Recently, there has been speculation that all of the data concerning post-ESWL hypertension is correlational[134] and therefore cannot establish causality.[135,136] This fact led Lingeman[137] to state: "the number 1 priority must be to establish whether ESWL causes hypertension."[138] This sentiment had already been expressed a month earlier in the literature by Mulley, Carlson and Dretler[139] who said, "The best estimates of the risk of hypertension that can be attributed to ESWL, or other stone removal techniques would come from a randomized control trial with careful long-term follow-up."[140] With this statement, the concerns expressed by Challah and Mays[141] appear justified.

(iv) End-Stage Chronic Renal Failure: Can it be Caused by ESWL?

With the demonstration by Bomanji[142] et al. that ESWL causes partial obstruction of the untreated kidney as well as the treated kidney (as measured by PTTI), and the demonstration by Williams[143] et al. that the changes in the treated kidney may not be temporary, the above question is a legitimate one. In a recent publication, Sofras[144] et al. show that renal failure occurred in one of their patients: "One patient progressed to chronic renal failure; this occurred in a bilaterally obstructed system which was treated on consecutive days."[145] These authors go on to list a rate of 0.05% for "renal failure" after ESWL.[146]

The key factor in the above case seems to be treatment by ESWL which is both "sequential" and "bilateral," within days of each other. This practice is not an unusual one for those physicians treating patients who are affected with stone disease bilaterally. Riehle, Fair and Vaughn[147] describe 25 patients (out of a total of 467 patients) who "received bilateral treatment; these were sometimes performed sequentially, with the patient under the same anesthesia."[148] Burns[149] et al. amplify this point when speaking of 104 patients (19%) in their series of 543 in which "both sides were usually treated even if the calculi were asymtomatic on one side."[150]

There are patients who are born with only one kidney (or lose a kidney surgically), form stones, and are treated by ESWL.[151] Ellis[152] et al. describe a child with end-stage renal disease (who had already rejected one transplanted kidney) who was treated by ESWL for renal calculus soon after the receipt of a second renal allograft. Locke,[153] et al. describe a similar instance of ESWL treatment to a transplanted kidney in a 51-year-old man.

(v) ESWL-Related Deaths with the Dornier Models

In spite of the coupling of lithotripter to cardiac cycle (by way of the ECG), there have been deaths of patients undergoing ESWL with the Dornier Models. These deaths can be subdivided into "ESWL-related" and "ESWL-unrelated" mortalities. The Cooperative Study done in the U.S. registered 4 deaths, 2 of which were ESWL-related (cerebrovascular accident and hypertension) in the treatment of 2,112 patients.[154] Charig[155] et al. report 2 ESWL-related deaths over 80,000 patients treated world wide (these 2 deaths are not the ones mentioned in the Cooperative Study).

The death recorded in the clinical testing of the Dornier Model HM1 is an interesting one because it was listed as ESWL-unrelated when in fact (according to this author) it appears to be ESWL-related.[156] Granted that this death occurred in a 70-year-old man with a heart condition, but if he had not been required to go in and out of the water bath during ESWL, it is highly likely that this man would not have had a cardiac arrest and died; at least at that point in time.

Sofras[157] et al. experienced 2 cardiac arrests amongst the 2,000 patients they treated using ESWL that could easily have died but are said to have "recovered."[158] It is necessary to state again (at least in the case of the Dornier Model HM3) that some patients, although they are few in number, die while having their renal calculi treated by ESWL.

(vi) The Question of Efficiency

One of the great problems in doing any kind of analysis of the publications pertaining to ESWL for treatment of urolithiasis is that presently (and in the past) each author defines "successful treatment" independently, therefore making interinstitutional comparisons very difficult. There is no way of ascertaining whether differences between the 91.8% success rate quoted by the London Stone Clinic[159] and the 68.4% success rate quoted by Sofras[160] et al. are caused by different definitions of "success," different techniques of ESWL, differences in patient populations, or differences in ESWL-related expertise of the authors. Only Lingeman[161] et al. define "clinically insignificant residual fragments,"[162] allowing a reader some idea of what a successful treatment must encompass (i.e., a treatment which leaves no fragments or only clinically insignificant residual fragments).

What is clear in assessing ESWL is that three features of this new technology very much affect its efficiency (cost-effectiveness). These features are:

(1) The rate of success of patients treated with ESWL (i.e., the percentage that become stone-free after one treatment),

(2) The number of patients requiring more than one ESWL treatment for the same stone, and

(3) The use of adjunctive urological procedures (eg.,

cystoscopy, placement of ureteral stents,[163-166] etc.) that may, or may not accompany stone treatment with ESWL.

These three features show tremendous variance from institution to institution.

The success rates of 91.8% and 68.4% (quoted previously) represent the highest and lowest rates, respectively, found by the author in a literature review encompassing 1982 to the present day (1989). Obviously there are many extraneous factors in a comparison such as this (see above discussion) including the type and size of the stones that the authors attempt to treat by ESWL. The U.S. Cooperative Study found that 77.4% of stones treated with ESWL in their study had passed completely 3 months following treatment.[167] Lingeman[168] et al. found that 3 months after ESWL, 72% of their patients were completely free of stone and another 24% had clinically insignificant residual fragments (which sums to a total of 96% of all the patients they treated).

Regarding repeat ESWL treatments (point 2 above), the Cooperative Study found that 16% of their patients required ESWL more than once.[169] The corresponding number of Lingeman[170] et al.'s group was 10%. Regarding adjunctive urological procedures (point 3 above), the Cooperative Study found 17% of their patients required adjunctive urological procedures[171] while Lingeman et al. found a total of 15.5% in their study.[172] There is tremendous variance for this factor in the literature varying all the way from 0.7% reported by Chaussy and Schmiedt[173] to 23.4% reported by Jansen[174] et al.

An excellent example of factors involved in the preceeding discussion becoming actualized, is provided by Burns, Breaux, and Crowe,[175] who described a study of ESWL at their institution in which 543 patients were treated. Of this total number, 81 (14.9%) patients required "a secondary procedure" (an adjunctive urological procedure), 35 (6.4%) patients required another ESWL treatment for the same stone (a repeat of ESWL), and 47 (7.9%) required pre-ESWL placement of ureteral stents (to help the kidney with drainage into the bladder) which is an adjunctive urological procedure. These figures sum to a total of 163, or 29.2% of the population undergoing ESWL treatment at that institution who needed "something else" in addition to the one treatment of ESWL they received. It is to be noted that the 3 patient divisions, and percentages, are not mutually exclusive and therefore some of the patient population will be counted twice in a calculation such as this. But it appears (based on this study), that probably 25% of patients undergoing treatment of their renal calculi with ESWL and utilizing the Dornier Model HM3 lithotripter, will require another procedure of some type; with its attendant cost. **Table 6** is a comparison of the effects of the three modalities of treatment for urolithiasis that have been highlighted in this thesis.

TABLE 6

Effects of Open Surgery, PCNL and ESWL
for the Treatment of Urolithiasis.

	Open Surgery	PCNL	ESWL by HM3
Days in Hospital	7-10	5.2-7.0	0-7
Disability Days	4-6 wks	1-2 wks	1-7 days
Mortality	0.38-1.5%	.001-.046%	.000025%
Complications	loss of renal function after repeated surgeries 2%	all 10.8%	new onset of hypertension[17] - 8.2% and hypertensive sequelae decreased renal function acute[76] - 16.2% chronic[84] - 24% subcapsular perirenal bleeding[22] - 0.66-3.8%
Success Rate	96%	97-98.3%	68.4-91.8%
Other			repeat ESWL or complementary surgical procedure[3,149] 15.5-25%

V. Bioeffects of the "Lithostar"

It must be pointed out at this time that nearly all of the studies referenced to this point in the presentation concern and refer to ESWL utilizing the Model HM3 Lithotripter which is a first generation lithotripter manufactured by Dornier Medical Systems, Inc. Both hospitals in Alberta that are acquiring ESWL technology have opted for the "Siemans Lithostar," manufactured by Siemans Medical Systems, Inc.

Both companies are based in West Germany (F.R.G.).

As has been demonstrated, much of the recent literature concerning the HM3 has not been favorable. But what about the Lithostar? Does it show any improvement in the bioeffects discussed? Can better results be expected with it? Is it more efficacious and effective? Although fragmentary evidence exists presently, because of the newness of second generation technology, the literature appears to show that the bioeffects related to the Lithostar are not as numerous and not as severe as the Dornier Model HM3.

The OHTA found an incidence of ESWL-related hypertension of 4.3% in their study of the Lithostar.[176] This is roughly half the rate of 8.2% reported by Lingeman and Kulb[177] in 1987 with use of the Model HM3. Other than the OHTA's report, no published report could be found, at time of writing, which pertained specifically to post-ESWL hypertension related to the Lithostar.

Recently, McClennan and Clayman[178] reported results in treating 266 patients for urolithiasis utilizing the Lithostar. They found an initial stone disintegration rate of 89% but a stone-free rate of only 57% three months post ESWL. Their rate for adjuvent urological procedures for this lithotripter was 12% as well as a rate of 6% for patients requiring more than one ESWL treatment. They found that 95% of their patients were able to be treated on an outpatient basis using the Lithostar.[179]

Scharfe[180] et al. found a stone disintegration rate of 96% using the Lithostar, but quote no post-ESWL stone-free rate. These researchers found a rate for subcapsular hematoma that was "related often to untreated hypertension and was seen in 0.3% (of the patients in their study)."[181] Psihramis[182] et al. report a rate in Toronto for repeat ESWL of 11% using the Lithostar, and an overall stone-free rate after three months of 41%.

The data concerning second generation lithotripers is as yet clearly preliminary. Based on what is presently in the literature, however, it appears that the number of bioeffects related to these machines has gone down,[183,184] but at the cost of a greater number of shock waves required to do the job, coupled with a larger number of secondary treatments.[185] The evidence is still too fragmentary to ascertain the effects on the overall cost of second generation over first generation technology.

ENDNOTES -- CHAPTER V

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using pigs and in humans by Preminger[165] et al. which addresses the fact that rather than promoting drainage, these stents "may not contribute to a higher rate free of stones ... and, in fact, make the treatment more uncomfortable for the patient than performing lithotripsy without ureteral stenting.[166]

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CHAPTER VI

PROTECTING THE MEDICAL COMMONS: THE MECHANISM AS IT NOW STANDS

The first five chapters of this presentation chronicle the painstaking development of a new method (ESWL) for the treatment of urolithiasis. This development has been followed from inception, development and testing, through to widespread implementation, and diffusion throughout the health care systems of the Western world. In the last chapter (Chapter V), evidence was presented which begs the question: "What are the effects of this new method of treatment (technology) on patient health status?" The second question (Chapter II) posed by Sackett,[1] "Does it work?" remains unanswered.

With no suitable answer to the question, another question now must be asked: "Who speaks (officially) for the interests of the Canadian public?" The question is "double-barreled." It concerns the questions of safety (of a technique which has still not undergone an RCT of any kind), and expense (the lithotripter being installed at the Edmonton Misericordia Hospital will cost between two and three million dollars before becoming operational[2-4]). As health care resources become increasingly scarce, Hiatt[5] asks the question "Who is responsible for protecting the medical commons?"

As has been previously mentioned (Chapter I), data has been solicited, received, and assembled in an attempt to answer the question of what societal mechanism(s) is (are) in place presently, to "assess, approve, ratify and implement new medical technologies as they appear on the Canadian scene,"[6-8] focussing on the technology of ESWL as an example. The answer to this question is in three parts. The mechanism in place in the United States is briefly described, followed next by that of Canada, and finally that of Alberta. The final chapter in this presentation presents the author's assessment of mechanisms in place in Canada and in Alberta. Following this, recommendations will be made for possible improvements of this system.

I. The American Mechanism

The American mechanism for approval of new technologies is vested in the USFDA. Once approval is given by this body to permit such a technology to enter the U.S. health care system, the OHTA is often approached by the Health Care Financing Administration (HCFA) pertaining to the appropriateness of placement of the new technology on U.S. Medicare and/or Medicaide formularies.[9] The OHTA, "considers the safety, efficacy and effectiveness, and, as appropriate, the cost-effectiveness and appropriate uses of the technology."[10] The essence of the job given to the OHTA is "to advise the Secretary of the Department of Health and Human Services respecting health care technology issues ..."[11]

The assessment process of the OHTA takes place in four stages: (1) Initiation (the formal request to evaluate), (2) Collection of Information (presently using the MEDLARS

II Computer System), (3) Synthesis of Information, and (4) Distribution of Results.[12]

The experience of the author in talking with the OHTA has been a very favorable one and they have provided him with three of their summaries concerning ESWL for use in this presentation.[13-15]

II. The Canadian Mechanism

In Canada, the legislation pertaining to the regulation of new medical technologies falls under The Food and Drugs Act[16] and the mechanism is much different from that of the American system. Whereas the USFDA has complete power (barring Court challenge) to sanction or not sanction a technology, in Canada, "there is no authority or mechanism under The Food and Drug Act to approve a medical device prior to its sale in Canada. It is the responsibility of the manufacturer to ensure that the regulatory requirements are met."[17] This fact was confirmed by personal communication between the author and the Minister of National Health and Welfare, who stated "The Department of National Health and Welfare does not approve medical devices or the associated technologies. Rather, it is the manufacturer's responsibility to ensure that medical devices which he sells are safe and efficacious when used as directed."[18] Reference to Section 14 of the Medical Devices Regulations made pursuant to the Food and Drugs Act shows that the Minister is correct with his interpretation. Section 14 states:

> No manufacturer of a device or person who has imported into Canada a device for sale shall sell the device unless tests have been conducted in respect thereof and the tests indicate that the nature of the benefits claimed to be obtainable through the use of the device and the performance characteristics claimed for the device are justified as shown by evidence available in Canada to the manufacturer or the person importing the device.[19]

Clearly the onus is on the manufacturer to establish safety to the public once the device is introduced into the marketplace.

The public is not left without any protection. Canada has a health protection bureaucracy called the "Health Protection Branch" (HPB), which functions in roughly an equivalent fashion to the USFDA but more at "arms length" than the American body. Part III of the Medical Devices Regulations deals with establishing safety of new medical devices. Section 28(1) states:

> The Director (of the HPB) may, in writing, request the manufacturer of a device to submit to him, on or before a specified day, evidence to establish the safety of the device under the conditions under which the device is recommended for use and the effectiveness of the device for the purposes recommended.[20]

Subsections (2) and (3) of Section 28 go on to state the sanctions which are at the Director's disposal if the manufacturer does not comply with this request, or if "the evidence submitted by a manufacturer pursuant to Subsection (1),"[21] does not clearly establish safety of the device to the satisfaction of the Director. These sanctions include complete removal of the device or technology from the Canadian health care system and marketplace.

More importantly, for the purposes of this presentation, are the provisions of the Regulations which encompass the term "new device." A technology considered to be a new device is subject to Part V of the Regulations which requires the manufacturer, pursuant to Section 34(a) of the Regulations, to acquire a pre-market review in the form of "A Notice of Compliance" from the HPB.[22] In obtaining such a notice, the manufacturer may be required to perform "clinical trials" as discussed under Section 35(3) of the Act.[23] These clinical trials do not have to employ randomization, however, "we encourage them to be randomized whenever possible and ... we focus more on number of people in the clinical trial, as well as the duration of the trial."[24] Even if a device is designated a "new device," RCTs are not, by Canadian law, necessary for sale of the device in Canada.

On the whole, if a new technology is subject to Part V of the Regulations, the adjudication of the manufacturer's request is more rigorous, but still does not require RCT.

Section 32 defines a new device as "a device listed in the Table to this Part ..."[25] The Table in question is Table 7 reproduced on the next page.[26]

TABLE 7

"New Devices" as Defined by the Food and Drugs Act[23]

1. Contact Lenses designed or represented for prolonged wear.
2. Menstrual tampons.
3. Any device designed to be implanted into the tissues or body cavities of a person for 30 days or more.

As may be clearly seen, by the terms of this Act, the lithotripter does not qualify as a "new device." It does not require either a pre-market review before entry into the Canadian health care system, nor does it require (by law) that clinical trials be done. It is not subject to Part V of the Regulations but rather the more lenient Section 14 and its corollaries.[27,28]

III. Provincial Mechanisms: The Case of Alberta

From the time of Confederation, health status and the health care of the people has been a provincial responsibility.[29] This has left each province free to enact its own legislation pertaining to health care. In this way, Canada is a very loose coalition of eleven individual health schemes; the eleventh being the health care of native Canadians which is a responsibility of the federal Government.[30]

The evolution of ESWL into Alberta is an interesting one.

In August of 1986, an interdisciplinary committee comprised of urologists, radiologists, and hospital administrators submitted its report to Alberta Health as had been requested by the latter. This report called for the purchase of two lithotripters by the Province.[31]

In an interview with the person placed "in charge" of ESWL-implementation by the Province, the author asked "What mechanism does the Government of Alberta have in place to assure the safety of the Public regarding ESWL?" to which he was told, "We don't have a mechanism."[32]

Protecting the safety of the Public from the use of improper medical techniques, devices, and/or practices lies outside of Government and with the the Council of the College of Physicians and Surgeons (of Alberta) pursuant to The Medical Profession Act[33] enacted by the Alberta Legislature. Regarding new medical technologies in general, the Registrar of the College states:

> The Council of the College of Physicians and Surgeons does not investigate every new modality in medical technology unless there is a specific reason to do so.[34]

In the case of the lithotripter, specifically, he states that:

> The Council has not made a study into whether lithotripters are efficacious, efficient or safe.[35]

By August, 1988, definitive steps were being taken by the Province to prepare for the implementation and diffusion of

ESWL within the boundaries of Alberta. The sites chosen for implementation were the Misericordia Hospital of Edmonton and the Holy Cross Hospital of Calgary.[36] The provincial Government appears to have taken for granted the efficacy, effectiveness, and safety of this technology. It appears that Government attentions have focussed more on logistics, equity, and the establishment of a means of treating patients in the province of Alberta, with what the Government sees as an efficacious, effective, and safe new technology for the treatment of urolithiasis. However, as Lingeman so carefully pointed out in 1988 at the Annual Meeting of The American Urological Association:

> It should be recognized that the rapid acceptance and adoption of ESWL has been facilitated, in part, by the false perception that this technology is entirely safe ...[37]

The safety of ESWL was never questioned by the Government of Alberta. This responsibility was felt to lie outside of Government with The Council of the College of Physicians and Surgeons of Alberta. As Hiatt asks:

> Who is responsible for protecting the medical commons?[38]

The reader now has the full story of the development, testing, implementation and diffusion of the new technology of ESWL into Alberta. The reader must now ask himself, "Has the system worked? Would I (the reader) feel comfortable having my kidney stone(s) treated by ESWL? As further new health technologies appear on the scene," as indeed they will, "can I rest assured that a system is in place in Canada, and in Alberta, such that, only those technologies which are efficacious, effective, and safe get through into the system?" In short, when it comes to the implementation of new health care technologies:

Should the status quo be maintained?

ENDNOTES -- CHAPTER VI

1. David L. Sackett, "Evaluation of Health Services," in Public Health and Preventive Medicine, 11th ed., edited by John M. Last (New York: Appleton-Century-Crofts, 1980), p.1800.

2. Donald J. Philippon (Assistant Deputy Minister, Hospital Services Division) to Gerry Hiebert (President, Misericordia Hospital), 12 January 1989, Edmonton, Appendix C to this Thesis.

3. William Steinberg, "Extracorporeal Shockwave Lithotripsy: Human Resource, Supplies Budget and Associated Impact Areas," study carried out by Misericordia Hospital in-house task force, Edmonton, November 1988.

4. Lawrence C. Wiser, "A Time for Reflection: a Prospective Cost-effectiveness Study of Lithotripsy in Northern Alberta," a paper written in partial fulfillment of the requirements for Health Services Administration 571, a postgraduate class in health care economics at the University of Alberta, Jan. - April 1989.

5. Howard H. Hiatt, "Protecting the Medical Commons: Who is Responsible?" The New England Journal of Medicine 293 (31 July 1975): 235-41.

6. Lawrence C. Wiser to The Honourable Perrin Beatty (Minister of National Health and Welfare), 24 February 1989, Appendix A to this Thesis.

7. Lawrence C. Wiser to The Honourable Nancy Betkowski (Minister of Health, Province of Alberta), 24 February 1989, Appendix A to this Thesis.

8. Lawrence C. Wiser to Donald Goldstone, M.D. (Acting Director, U.S. Office of Health Technology Assessment), 24 February 1989, Appendix A to this Thesis.

9. United States Department of Health and Human Services, National Center for Health Services Research Office of Health Technology Assessment (Rockville, Maryland: U.S. Public Health Service, 1988), p.3. This is a pamphlet provided by the Center to explain their functions.

10. Ibid., p.2.

11. Ibid.

12. Ibid., pp.5-6.

13. United States Department of Health and Human Services: National Center for Health Services Research and Technology Assessment, Summary of Safety and Effectiveness Data: Dornier Lithotripter, Model HM3 (Rockville, Maryland: U.S. Public Health Service, 1985).

14. Idem, Summary of Safety and Effectiveness Data: Siemans Lithostar Lithotripter (Rockville, Maryland: U.S. Public Health Service, 1988).

15. Idem, Summary of Safety and Effectiveness Data: Medstone Model 1050 ST Lithotripter (Rockville, Maryland: U.S. Public Health Services, 1988).

16. Food and Drug Act, R.S.C. 1985, c.F-27, s.30.

17. Canada, Health Protection Branch, Guide to the Preparation of a Submission to Part V of the Medical Devices Regulations (Ottawa: Minister of National Health and Welfare, 1984), p.3.

18. The Honourable Perrin Beatty (Minister of National Health and Welfare) to Lawrence C. Wiser, 29 March 1989, Appendix B to this Thesis.

19. Medical Devices Regulations, C.R.C. 1978, c.871, s.14.

20. Idem, C.R.C. 1978, c.871, s.28(1).

21. Idem, C.R.C. 1978, c.871, s.28(3).

22. Idem, C.R.C. 1978, c.871, s.34(a).

23. Idem, SOR/79-755.

24. S. Mohanna, M.D. (Chief, Clinical Advisory Division, Canadian Bureau of Radiation and Medical Devices, Ottawa), telephone interview by the author, Edmonton, 1240 - 1255 hrs., 28 July 1989.

25. Medical Devices Regulations, C.R.C. 1978, c.871, s.32.

26. Idem, SOR/82-914.

27. K.A. Hutcheon to Lawrence C. Wiser, 10 May 1989, Appendix B to this Thesis.

28. W. J. Welsh to Lawrence C. Wiser, 3 May 1989, Appendix B to this Thesis.

29. Constitution Act, 1867, (U.K.), 30&31 Vict., c.3, s.92(7).

30. Idem, 1867, (U.K.), 30&31 Vict., c.3, s.91(24).

31. Gordon Ward (project manager, ESWL implementation, Alberta Health) to Larry Wiser, 19 June 1989, Appendix B to this Thesis.

32. Gordon Ward, interview held at Hy Center, Edmonton, 6 April 1989.

33. Medical Profession Act, R.S.A. 1980, c.M-12, s.31.

34. Dr. L. H. LeRiche (Registrar, College of Physicians and Surgeons of Alberta) to Lawrence C. Wiser, 17 May 1989, Appendix B to this Thesis.

35. Ibid.

36. Op. cit. 31 above

37. James E. Lingeman, "The Role of Lithotripsy and its Side Effects," paper presented at the 83rd Annual Meeting of The American Urological Association, Boston, Mass., 3-7 June 1988, p.8. This is a statement that was mentioned in the first page of this presentation. The reader is in a better position at this point to appreciate the significance of Lingeman's comment in light of the actions of the Government of Alberta, as well as Canadian governments at all levels.

38. Op. cit. 5 above. The title of Hiatt's presentation is reframed in this question of the author, but the essence is the same; who is looking out for the public good?

CHAPTER VII

AN EXPLORATION OF THE COST ANALYSIS RELATED TO THE TREATMENT OF UROLITHIASIS BY ESWL

I. Method

It appears inevitable, that given the controversy and unanswered questions surrounding ESWL, a randomized clinical trial of ESWL will be done, eventually. If such an RCT were to show a lowering of patient health status, then clearly, the present day status of this technology would be lost very rapidly and the technology abandoned.

Perhaps a more intriguing question, however, would be what course of action should be followed if the above-mentioned RCT shows (as present day proponents fervently believe) a beneficial effect to those patients receiving ESWL for treatment of their kidney stones? In this scenario the questions of efficacy and effectiveness posed by Sackett,[1] would be answered affirmatively, and all researchers then would be free to concentrate (with a clear conscience) on the economic analysis of the technology of ESWL.

Drummond[2] et al. list four methods of economic analyses. These methods will be discussed sequentially in ascending order of complexity beginning with the simplest and ending with the most difficult.

(i) Cost-minimization Analysis

This analysis assumes that all the consequences of a particular treatment are identical. "The efficiency evaluation is then essential in a search for the least cost alternative."[3] Clearly, in the case of treatment of kidney stones utilizing ESWL, all the consequences of treatment are not identical and so a researcher would not opt for this form of analysis.

(ii) Cost-effective Analysis

In this analysis costs are related to a single common, desired effect on health outcome. In this fashion the costs in effecting a 10 mm.-Hg decrease in diastolic blood pressure in a population of hypertensives, or ensuring that no random blood sugar is above 180 mgm. - percent in a defined diabetic population, may be assessed to find the most economically efficient methods of achieving these ends.[4] A splendid example of a cost-effectiveness analysis is offered by Hull[5] et al. who studied the economic efficiency of methods for the prevention of fatal pulmonary embolism in patients undergoing surgery.

(iii) Cost-benefit Analysis

Whereas a cost-effectiveness analysis looks at costs related to a single desired health outcome, in cost-benefit studies the measures become more stark and cold. In this form of analysis the single criterion becomes dollars. "The results of such analyses might be stated either in the form of a ratio of dollar costs to dollar benefits, or as a single sum (possibly negative) representing tne net benefit (loss) of one programme over another."[6] Wiesbrod[7] et al. offer an illustrative example of a cost-benefit analysis pertaining to health care policy assessment.

As one reduces human endeavours (and lives) to dollar values, a number of implicit assumptions become necessary which many of those who advocate cost-benefit studies (in the opinion of the author) must be oblivious to. Drummond[8] points to these assumptions when he says about cost-benefit analysis that it

> tacitly accepts the assumptions of Paretian value judgement;[9] that individuals are the best judges of their own welfare, that the distribution of income is 'accepted' or that issues of distributive justice can be tackled separately, and that social welfare is a function of the welfare of the individuals who make up the society.[10]

When the value of peoples' lives is measured in terms of their ability to earn (dollars), the lives of the very old and the lives of the very young become (by definition) worth "less." The uniqueness of health care creates problems in using the cost-benefit model as a means of economic assessment. These problems are noted by Evans,[11] who in pointing out the "cold, hard" facts of the cost-benefit analysis states:

> The elderly living on pensions and other assets, have earned no income and are therefore worthless. (They may be credited with some non-market production of rather ill-defined value in a more sophisticated analysis.) Children are worth something, but their future product is discounted back to the present and thus, for very young children particularly, becomes very small. Earnings of women, in most cultures, are below those of men, so the value of saving a woman's life is correspondingly lower. Unemployed time

> is worthless, so value of life must be adjusted for expectation of unemployment. In the United States, blacks earn less on average than whites, so blacks are worth less. Specific examples of these powerful value judgements, masquerading as objective quantitative analysis, can be found in the cost-benefit literature.[12]

The problem Evans is addressing is a fundamental one. If "benefits" are less than "costs," does one "scrap the capital," which is what this economic model is designed to answer; the "capital" in this case being human beings. Unless society is prepared to practice "active" euthanasia when the costs of a human life exceed the benefits of that life in monetary terms, there is no point in using this form of economic analysis to evaluate health care programs or technologies.

(iv) Cost-utility Analysis

This measure is considered by many to be the most complex, but also one of the most useful means of economic analysis.

> In cost-utility analysis... the incremental cost of a programme, from a particular viewpoint, is compared to the incremental health improvement attributable to the program, where the health improvement is measured in quality-adjusted life-years (QALYs) gained. The results are usually expressed as a cost per QALY gained.[13]

The great step forward that cost-utility analysis offers is that it is able to measure the economic utility[14] (i.e., satisfaction, well-being, value) attached by the patient to recovery from an illness or disorder. In doing this it is able thus "to incorporate simultaneously both the increase in quantity of life (reduced mortality) and the increase in the quality of life (reduced morbidity)."[15] However, one of the greatest challenges of cost-utility analysis is the establishment, weighting, and measurement of a utility-index which is creditable.

Drummond et al. list five situations in which cost-utility analysis should be used in the economic evaluation of a health care programme, treatment, or technology.[16] Briefly summarized they are:

(1) When quality of life is **the** important outcome.

(2) When quality of life is **an** important outcome.

(3) When the programme (treatment or technology) affects both morbidity and mortality and you wish to have a common unit of outcome that combines both effects.

(4) When the programmes (treatments or technologies) being compared have a wide range of different kinds of outcomes...

(5) When you wish to compare a program to others that have already been evaluated using cost-utility analysis.

II. Economic Analysis of ESWL

(i) Cost-effectiveness of ESWL

A study by Labelle[17] et al., published in 1987, presented a cost-effectiveness analysis of the treatment modalities for urolithiasis. It examined surgery, PCNL[18] and ESWL in the Central West Region of Ontario (Hamilton). Efficacy and effectiveness of ESWL were assumed to be present for this modality, and no RCT results are mentioned by the authors. Costs included in the study were related to: fees (both professional and technical), operating costs, and hospitalization costs of each of the three methods of treatment. **Table 8** and **Table 9** encapsulate their costing data. Not costed in this analysis were some of the capital costs involved: cost of the operating room, cost of radiological procedures, cost of the adjuvant procedures related to ESWL, etc. The results of their cost-effective study is provided by **Figure 6**. **Table 9** shows effects of the three treatment modalities in terms of disability days.

FIGURE 6

Cost per Patient as a Function of the
Annual Number of ESWL Procedures[17]

Figure 6 not available due to copyright restrictions.

TABLE 8

Cost Compilation of Study by Labelle[17] et al.

Table 8 not available due to copyright restrictions.

TABLE 9

Incremental Analysis of Costs and Effects[17] ($ Cdn. 1985)

Table 9 not available due to copyright restrictions.

A critical assumption in Labelle et al.s analysis was the assumption of the efficacy and effectiveness of ESWL.

Recent studies by Lingeman and Kulb[19] and by Knapp and Kulb[20] have shown that the assumption of efficacy and effectiveness of ESWL is open to question. These studies demonstrated post-ESWL hypertension and perirenal hematoma.

(ii) Cost-utility of ESWL

The fact that post-ESWL-related hypertension will affect the ESWL treated person over his or her lifetime, and the fact that, in Canada, it is the provincial government that must pay these costs, are costs not captured by Labelle et al.'s arbitrary five-year cost-effectiveness analysis. Also not weighted by these authors is the cost of the patient in personal terms, and in terms of his or her enjoyment and/or satisfaction (utility) of life. These are measures (quantity and quality of life) accounted for only by cost-utility analysis of ESWL.[21] Such a presentation of costs must be taken into consideration even though these costs occur years "downstream." Regardless of when they occur, these are significant costs, and are pointed out in the following section of this chapter which deals with hypertension.

Secondly, as the technology of ESWL has evolved, the frequency of PCNL has not decreased, but in fact, has increased.[22,23] ESWL is clearly not the economic "substitute" for PCNL as first thought, but rather an economic "complement" to it, with attendant economic costs.[24,25] This is seen no more obviously than in the "hybrid" method of treatment for urolithiasis which utilizes PCNL to first "debulk" or shave a large kidney stone, before proceding on with ESWL. Any future form of economic analysis must account for these costs if true accuracy is the goal of such a study.

McKinlay,[26] in 1981, listed the seven stages of "the typical career of a medical innovation."[27] They are:

(1) promising report

(2) professional and organization adoption

(3) public acceptance and state (third-party) endorsement

(4) standard procedure and observational reports

(5) randomized controlled trial (RCT)

(6) professional denunciation

(7) erosion and discreditation.

Based on these observations and pertaining specifically to the treatment of urolithiasis utilizing ESWL, it would appear that we are presently between steps 4 and 5, with the remaining steps yet to occur. Had efficacy and effectiveness been established first, before implementation and diffusion of ESWL, this whole process (with its attendant cost in resources) could have been avoided.

III. **ESWL-related Hypertension**

As an epilogue to this discussion, the reader is reminded that some ESWL-related costs (which are part of the cost to society of using ESWL) do not present themselves at the time of treatment, but years later. These costs may be very substantial, enough to shift the cost-curve of **Figure 6** significantly to the right. The author is referring to the bioeffects created by ESWL, predominantly the post-ESWL-related hypertension and its sequelae. What is the cost to society of shortening an able-bodied person's life by 10 to 20 years because of ESWL-related-hypertension? One highly respected text of Internal Medicine[28] has the following to say about the condition of hypertension:

> the probability of developing a morbid cardiovascular event with a given arterial pressure may vary as much as twentyfold depending on whether associated risk factors are present... it has been documented that untreated hypertension is associated with a shortening of life by 10 to 20 years, usually related to an acceleration of the atherosclerotic process... Nearly 30 percent will exhibit atherosclerotic complications, and more than 50 percent will have end organ damage related to hypertension itself, e.g., cardiomegaly, congestive heart failure, retinopathy, and cerebrovascular accident and/or renal insufficiency.[29]

These are the hidden liabilities and costs of ESWL not accounted for by Labelle et al. in their study. Quite simply they are the hidden liabilities and costs of implementing any new technology without benefit of first doing a randomized clinical (control) trial.

ENDNOTES -- CHAPTER VII

1. David L. Sackett, "Evaluation of Health Services," in Public Health and Preventive Medicine, 11th ed., edited by John M. Last (New York: Appleton-Century-Crofts, 1980), p. 1800.

2. Michael F. Drummond, Greg L. Stoddart and George W. Torrance, Methods for the Economic Evaluation of Health Care Programs (Toronto: Oxford University Press, 1987), pp. 10-16.

3. Ibid., p. 10.

4. Ibid., p. 11.

5. Russel D. Hull et al., "Cost-effectiveness of Primary and Secondary Prevention of Fatal Pulmonary Embolism in High-risk Surgical Patients," Canadian Medical Association Journal 127 (15 November 1982): 990-95.

6. Op. cit. 1 above, p. 12.

7. Burton A. Weisbrod, Mary Ann Test and Leonard I. Stein, "Alternative to Mental Hospital Treatment," Archives of General Psychiatry, 37 (April 1980): 400-05.

8. Michael F. Drummond, "Welfare Economics and Cost Benefit Analysis in Health Care," Scottish Journal of Political Economy 28 (17 February 1981): 125-45.

9. Edgar K. Browning and Jacqueline M. Browning, Microeconomic Theory and Applications, 2nd ed. (Toronto: Little, Brown and Co., 1986), pp. 148-53. The "Paretian value judgement" spoken of by Drummond is related to the concept of "economic efficiency" taught by the Italian economist Vilfredo Pareto (1848-1923) a century ago. It is more frequently referred to today as "Pareto optimality." Briefly and simply stated, it refers to an "efficient" distribution of goods between two (or more) people. "An efficient distribution of fixed total quantities of goods is one in which it is not possible, through any change in the distribution, to benefit one person without making some other person worse off" (Browning et al. above, p. 149). In this situation all parties have attained maximum utility (satisfaction, value) from the fixed quantity of goods available.

10. Op. cit. 8 above, p. 126.

11. Robert G. Evans, *Strained Mercy* (Toronto: Butterworths, 1984).

12. Ibid., pp. 253-54.

13. Op. cit. 2 above, p. 112.

14. Richard G. Lipsey, Douglas D. Purvis and Peter O. Steiner, *Economics*, 5th ed. (New York: Harper and Row, 1985), pp. 110-15.

15. Op. cit. 2 above, p. 113.

16. Ibid., pp. 113-14.

17. R. J. Labelle et al., "Economic Evaluation of Extracorporeal Shock Wave Lithotripsy, Percutaneous Ultrasonic Lithotripsy, and Standard Surgical Treatment of Urolithiasis - a Canadian Perspective," *Clinical and Investigative Medicine* 10 No. 2 (19878): 86-95.

18. Ibid. The authors of this article speak of Percutaneous Ultransonic Lithotripsy (PUL) which is simply the debulking of a kidney stone through a percutaneous approach. It is the same procedure as PCNL and while these authors prefer to speak of PUL in their article, practically speaking, there is no difference. The author has used the terms PCNL and PUL interchangeably in this Chapter.

19. James E. Lingeman and Thomas B. Kulb, "Hypertension Following Extracorporeal Shock Wave Lithotripsy," *The Journal of Urology* 137 No. 4, Part 2 (April 1987): 142A, abstract 154.

20. Peter M. Knapp and Thomas B. Kulb, "Extracorporeal Shock Wave Lithotripsy Induced Perirenal Hematomas," *The Journal of Urology* 137 No. 4, Part 2 (April 1987): 142A, abstract 155.

21. Op. cit. 1 above, pp. 113-114.

22. William H. Bush et al., "Impact of Extracorporeal Shock Wave Lithotripsy on Percutaneous Stone Procedures," *American Journal of Roentgenology* 147 (July 1986): 89-93.

23. Andrew J. Leroy et al., "Percutaneous Renal Calculus Removal in an Extracorporeal Shock Wave Lithotripsy Practice," *The Journal of Urology* 138 (October 1987): 703-06.

24. Op. cit. 9 above, p. 88.

25. Op. cit. 14 above, pp. 49-50.

26. John B. McKinlay, "From 'Promising Report' to 'Standard Procedure': Seven Stages in the Career of a Medical Innovation," Milbank Memorial Fund Quarterly 59 No. 3 (1981): 374-411.

27. David Feeny, Gordon Guyatt and Peter Tugwell, eds., Health Care Technology: Effectiveness, Efficiency and Public Policy (Montreal: The Institute for Research on Public Policy, 1986), p. 10.

28. Eugene Braunwald et al., Harrison's Principles of Internal Medicine, 11th ed. (Toronto: McGraw-Hill Book Co., 1987), pp. 1024-26.

29. Ibid., p. 1026.

CHAPTER VIII

PROTECTING THE MEDICAL COMMONS: CONCLUSIONS AND RECOMMENDATIONS

This presentation has demonstrated that solid and accepted mechanisms exist regarding economic evaluation of a new medical technology delivered into a health care system (Chapters II and VII). It has stressed, however, that before embarking on an economic analysis of such a technology, two questions must be answered affirmatively, or such an analysis is unwarranted.[1]

Though now widely implemented and diffused, there is no scientific evidence (established by RCT) that ESWL, in the treatment of urolithiasis, works (i.e., is efficacious, effective, and safe).

The second question posed by Sackett[2] ("Does it work?") is still very much alive. This was never more clear than in a presentation[3] before the 1988 Annual Conference of The Americal Urological Association: "the rapid acceptance and adoption of ESWL has been facilitated, in part, by the false perception that this technology is entirely safe ... numerous clinical and experimental reports present evidence that ESWL can cause severe, acute effects."[4]

In a personal communication to the author,[5] Lingeman noted "the most important issue needing to be addressed regarding ESWL remains not who can be treated, but rather who should be treated with this exciting new technology."[6]

Responding to the perceptions by some[7] that PCNL may be more efficacious than ESWL for all but the simplest of stone problems, this ESWL-pioneer responded, "prospective randomized clinical trials of ESWL versus percutaneous nephrostolithotomy are probably the best way to examine the relative efficacy, cost, and morbidity of these two forms of treatment for nephrolithiasis."[8]

The above response of Lingeman, stands in sharp contradistinction to the response of the Registrar of the body enfranchised by statute with public safety in this domain (The Council of the Alberta College of Physicians and Surgeons), who states "The Council has not made a study into whether lithotripters are efficacious, efficient or safe."[9] It would appear that to the College at least, Sackett's question has been answered ("It does work!"), and no further study is contemplated.

If, after reading Chapter V of this presentation and the preceding two paragraphs, the reader feels somewhat confused, he or she should not feel badly. This is precisely the point. No definite position can be taken regarding ESWL because the definitive study that would answer the question of effectiveness, an RCT, has not been done. Until such a study is done, each person will see what he/she wants to see regarding the use of ESWL. If a proper RCT study would have been done prior to the release of lithotripters into the Canadian health care system, the question would be moot. It is true, that Canadians may have had to be denied a valuable technology (for a while, while lithotripters proved their effectiveness) and utilized resources in doing the study, however, the question of effectiveness ("Does it work?") would have been forever answered, and the present debate pointless. Clearly the choice Canadian health care policy makers had to make, was between waiting for one to two years (or longer) with a reasonable expectation of knowing what the consequences of this new technology were, or waiting for one to two years, and still nct knowing.[10] The choice they made is painfully obvious.

I. The Picture at the Federal Level Regarding New Medical Technologies

(i) Conflict of Interest

It is made abundantly clear in The Food and Drugs Act, that the Government of Canada has great faith that the manufacturers of new medical technologies will hold the safety of the Public above their desire for profit. But recent publications within the last twelve months appear to indicate that this strategy may be at best unwise, and probably dangerous.

When public safety is entrusted to a multinational corporation (like Siemans or Dornier), the public finds itself in what Booth[11] describes as "an ethical no-man's land where the interests of academic science and business collide."[12] Booth is referring to an incident in which three members of the esteemed Harvard Medical School have been accused of "conflict of interest," and which has spawned several official probes.[13]

The Harvard conflict centers around a paper published by three faculty members in a reputable Ophthalmology journal[14] two months after they had received "exclusive rights" from the USFDA to market an eye cream for "Dry-eye Syndrome." This syndrome is a very unfortunate one which leaves the patient unable to produce tears to moisten his or her eyes.[15] In their publication, the Harvard trio of ophthalmologists claimed marvellous positive results following their treatment of Dry-eye Syndrome, which they attributed to a new eye cream they were using.[16] Not surprisingly, the trio did not mention in their article, that they held exclusive rights to this cream and stood to profit handsomely from its success.

Shortly after publication of this article[17] the stock price of the company which was manufacturing the cream in question went from 2 cents a share, the price at which the trio had "bought in" (an insider's price), to a peak of 8 dollars a share.[18] Recently, the results of a multi-center RCT in which the cream in question was compared to a placebo treatment of Dry-eye Syndrome were released,[19] and showed that "clinical symptoms and signs showed no significant improvement with active drug relative to placebo."[20]

In the wake of the scandal which followed, the Dean of The Harvard Medical School commented in a letter to his faculty, "There remains serious concern about how the institutional policies and procedures could have been bypassed to allow this flawed clinical study and conflict of interest to proceed without existing safeguards falling into place."[21] Can the same not be said concerning the present provisions in place to protect the Public in Canada's Food and Drugs Act? Regarding ESWL, is there not evidence that the Canadian Public has been trapped in "an ethical no-man's land?"

(ii) Scientific Fraud

Recent events in the U.S. scientific community have shown that "scientific fraud" is not an illusion.[22] The recent issuance by The Association of American Universities (AAU), of a general policy[23,24] to deal with "allegations of fraud, plagiarism, or other types of misconduct,"[25] indicates that the problem is real. So, too, does the establishment (under congressional pressure) by The National Institutes of Health (NIH) of an "Office of Scientific Integrity," to deal with such allegations.[26,27] Two NIH investigators of such misconduct report receiving 100 such allegations per year and they feel that "this number represents only the tip of a huge iceberg of cheating."[28] Such revelations recently caused U.S. Secretary of Health and Human Services, Louis Sullivan, to state "We are shocked by reports of scientific fraud,"[29] and that we must "rid ourselves of those who practice deception and fraud."[30]

Perhaps more interesting than the above revelations, and

Sullivan's response to them, was his explanation of why they are occurring. In it, the story (and fallacies) of ESWL are told:

> That which was once performed in the remote ivory tower of academia is now submitted to the glare of the television camera, the business investor, and the venture capitalist. The minute steps, the intricate minuet of scientific discovery, the start and stops of trial and error molecular modeling in our powerful computers are now reported instantly. The hopes and anticipation of the public soar to the heights or are dashed to the ground with the evening news.[31]

In this explanation, the pressures and the "mad rush" to implement and diffuse a technology such as ESWL can be felt and understood for what it is. Observations, similar to those just stated, prompted Ginzburg[32] to comment "technology need not necessarily result in progress, but may, in the absence of caution and restraint, prove a major threat ..."[33]

II. Recommendations and Conclusions

To summarize, a new technology has been developed abroad for the treatment of urolithiasis. It has been imported, implemented, and diffused within the Canadian health care system without scientific proof that it will positively affect the health status of those treated with it, and there is evidence that it may, in fact, lower the health status in a latent fashion of those treated. The province of Alberta has made a decision to purchase, implement, and diffuse two of these units at a cost of between 2 and 3 million dollars per unit.[34-36] Is this a wise use of precious and limited health care resources, and what other health care resources must be foregone in order to implement this technology?

The answer to the above question is one that all readers must inevitably ask themselves.

The question this presentation set out to answer was "What is the mechanism for assessing and approving, new 'embodied' health care technologies as they arrive on the scene in Canada?" This has been done. It is now time to make recommendations for improvement of "the system."

(i) Recommendations

RECOMMENDATION 1

That legislation be enacted, or amended, such that no new medical device may be offered for sale in the Canadian marketplace before proving its efficacy and effectiveness through "randomized clinical (control) trial." Such a provision would expand the definition of "new device" pursuant to Section 32 of the Medical Devices Regulations, whose present definition is so limited that it is effectively nonexistent.[37] Such legislation would ensure that no new health care technology would be implemented without full knowledge of its effect on patient health status.

In this way, it is felt that the use of resources on treatments that don't work, or may even harm patients, will be prevented. Milner[38] et al. point out that the "time window" in which RCTs may be comfortably done for ethical reasons is small, however, Chalmers[39] sees no reason not to randomize the first patient treated with any new technology.

RCTs are now done with the introduction of new drugs into the health care system with excellent results; albeit after the disaster of thalidomide. The present policy of the federal Government regarding new drugs as they enter the Canadian health care system is clear and does require randomization. A soon to be published federal Guideline regarding new drugs states:

> Control studies are studies in which potential variation has been appropriately stratified, and randomized to allow a direct meaningful comparison between two or more treatments.[40]

Surely there is no reason why similar rules should not apply to new "embodied" medical technology to extricate the system from what may well be a "pre-thalidomide" situation regarding new embodied technologies. Side effects arise from non-drug, as well as drug-based therapies.

RECOMMENDATION 2

That the federal Government take the lead in the establishment and the provision of centers where RCTs of new embodied technologies will be carried out and an assessment made into their efficacy and effectiveness. The establishment of such "technology centers" is recommended by Stiller[41] (who calls them "centers of excellence"). Such action would enable the federal Government in cooperation with the Provinces to re-establish leadership in health care matters,[42] and counter the charge by Gray[43] that "Ottawa ... is abdicating its traditional leadership role in health care."[44] It would also allow Governments at both levels to address a problem faced by all of Canada.

RECOMMENDATION 3

That the Government of Alberta and/or the Canadian Government accept responsibility for the analysis of the results of the RCTs emerging from the previously mentioned technology centers. If there is consensus that these results show significant positive effect on patient health status, then the responsible Government formally attest to this fact, and certify in writing that this is the case. This action is to be accomplished before implementation and diffusion of the technology into the country or province. In the present system, it would appear (initially at least) that the Goverment require the Council of the College of Physicians and Surgeons (through changes in the Medical Profession Act) be given this task of formally advising the Minister of Health of the efficacy and effectiveness of all new medical technologies. The final approval would, and should be given by the Province.

RECOMMENDATION 4

That the province of Alberta exercise caution in the establishment of ESWL technology and its diffusion into the Alberta health care system, and consider ESWL technology "experimental" pending the results of a provincial randomized clinical (control) trial supervised by the Province which will scientifically establish the fact that ESWL has a positive effect on the health status of those Albertans being treated with it. Such action should be implemented immediately, before positive media coverage of the new lithotripters begins. Once that occurs, the time window for RCT of ESWL will have closed and the technology of ESWL must be considered to be complete in terms of its diffusion into the Alberta health care system with all attendant costs borne by the population.

RECOMMENDATION 5

That the new system of technology assessment not be limited to new and/or embodied medical technologies. Medical treatments or technologies which may have doubtful or unknown efficacy (eg. routine fetal monitoring during labour; routine flexible colonoscopy for prevention of cancer of the colon; removal of asymptomatic gallstones) should be referred to the technology centers for scientific assessment.

RECOMMENDATION 6

That measures to ensure the appropriate use of ESWL (or any new medical technology) be mandated through Hospital and Peer Review reports of utilization of the technology. These reports will go directly to a standing committee (of varied clinical mix) struck by the College of Physicians and Surgeons to ensure the appropriateness of the technology's use.

RECOMMENDATION 7

That if and when ESWL, for treatment of urolithiasis, has proven (via an RCT) that it does enhance the health status of those undergoing this treatment, that consideration be given for study of the economic considerations of this technology by an economic analysis, and that that analysis be a cost-utility analysis incorporating as a treatment category the "hybrid" treatment incorporating the PCNL-ESWL mode of treatment as well as the costs of any "adjunctive" surgical procedures correlated with the use of ESWL for kidney stones.

RECOMMENDATION 8

That until a cost-utility analysis of ESWL is done, ESWL be considered an economic "complement" (additional cost) to treatments for urolithiasis already in existence previously, rather than the economic "substitute" (replacement) for these treatments which ESWL is currently being marketed as, and that a review of the effect of the economic unbundling associated with ESWL be done, before a new section is added to the fee schedule.

(ii) Conclusions

The above changes to the Canadian health care system are not small, and could not be implemented in their totality immediately. Over time, however, the savings from these measures could be substantial, especially when these measures are coupled with other recommended changes in the societal approach to health care exhibited by Canadians.[45]

In Canada, the provision of adequate health care is a right of citizenship ensured by statute.[46,47] Thus is created a finite medical "commons" available equally to each citizen upon the perception of illness. Hardin,[48] says of such a system, "Ruin, is the destination towards which all men rush, each pursuing his own best interest in a society that believes in the freedom of the commons. Freedom in a commons brings ruin to all."[49]

Hiatt[50] echoes these concerns when he says about "new medical practices" (technologies), "we risk reaching a point where marginal gains to individuals threaten the welfare of the whole."[51] He goes on to deplore "the utilization of precious resources for practices that benefit neither the individuals nor society, and that indeed are frequently harmful to both."[52] Clearly in these statements, is an implicit plea by Hiatt for efficacy and effectiveness in new medical practices (technologies).

In closing this presentation, which has used the new medical technology of ESWL as exemplary of all the new medical technologies of health care, the perceptions of Thomas[53] should be kept in mind. Lithotripsy, as a form of treatment for urolithiasis (it must be remembered) is a "half-way technology,"[54] as are all the new medical technologies; embodied or otherwise. "It is a characteristic of this kind of technology that it costs an enormous amount of money and requires a continuous expansion of hospital facilities."[55] We are progressing along the road to a "decisive technology"[56] for urolithiasis (like Salk's vaccine for polio) such that people will no longer form renal calculi,[57,58] or treatment by lithotripsy will become as effective and as simple as are our solutions for polio and smallpox.

In the intervening years, while we wait for this to occur, Government must be ever vigilant that the medical commons is protected and that nothing is implemented into the system that is not efficacious or effective. This is not now occurring.[59] The author has made recommendations that may help to achieve this. These recommendations, if implemented, also should decrease the number of "strained" confrontations which occur between health care professionals and government; for there is no point in asking to be provided with a new technology that does not improve patient health status, and it will be politically very difficult to deny one that does.

Perhaps then, there will be little need to fight. For both parties are partners in the same bed; the public good.

> Physicians must help gather and present as realistically and comprehensively as possible scientific and medical information ... and then join with a variety of other professionals, including statisticians, epidemiologists, economists, policy analysts, lawyers and ultimately politicians and the public in setting priorities.[60]

The Roman surgeon Celsus observed of his time, "That medicines and cures were first found out; and then, after, the reasons and causes were discoursed; and not the causes first found out, and by light from them the medicines and cures discovered."[61] Surely we, in our time, can make the same observations.

ENDNOTES -- CHAPTER VIII

1. The first question which must be answered affirmatively is "Can it work?" The second question is "Does it work?" A discussion of these two questions is dealt with in the first two pages of Chapter II.

2. David L. Sackett, "Evaluation of Health Services," in Public Health and Preventive Medicine, 11th ed., edited by John M. Last (New York: Appleton-Century-Crofts, 1980), pp.1800-23.

3. James E. Lingeman, "The Role of Lithotripsy and Its Side Effects," paper presented at the 83rd Annual Meeting of The American Urological Association, Boston, Mass., 3-7 June 1988.

4. Ibid., p.8.

5. James E. Lingeman to Lawrence C. Wiser, 6 June 1989, Appendix B to this thesis.

6. Ibid.

7. Nicholas Mays et al., "Clinical Comparison of Extracorporeal Shock Wave Lithotripsy and Percutaneous Nephrolithotomy in Treating Renal Calculi," British Medical Journal 297 (23 July 1988): 253-58.

8. Op. cit. 5 above.

9. Dr. L. H. LeRiche to Lawrence C. Wiser, 17 May 1989, Appendix B to this Thesis.

10. Peter Burney to the editor, British Medical Journal 292 (17 May 1986): 1333.

11. William Booth, "Conflict of Interest Eyed at Harvard," Science 242 (16 December 1988): 1497-99.

12. Ibid., p. 1497.

13. Ibid.

14. Scheffer C. G. Tseng et al., "Topical Retinoid Treatment for Various Dry-eye Disorders," Ophthalmology 92 No. 6 (June 1985): 717-27.

15. H. Kay Soong et al., "Topical Retinoid Therapy for Squamous Metaplasia of Various Ocular Surface Disorders," Ophthalmology 95 No. 10 (October 1988): 1442-46.

16. Op. cit. 14 above, p.726.

17. Op. cit. 14 above.

18. Op. cit. 11 above, p.1498.

19. Op. cit. 15 above.

20. Ibid., p.1442, abstract.

21. Daniel Tosteson (Dean of Medicine, Harvard Medical School) quoted in Booth above, p.1499.

22. Mark J. Poznansky, "Conflicts of Interest, Ethics and Fraud," Update Issue 8 (19 June 1989): 1. This is a local publication by the Faculty of Medicine of the University of Alberta, Edmonton.

23. Alun Anderson, "AAU Issues Guidelines on Dealing with Scientific Fraud," Nature 337 (19 January 1989): 196.

24. Colin Norman, "How to Handle Misconduct Allegations," Science 243 (20 January 1989): 305.

25. Ibid.

26. Joseph Palca, "NIH Change Procedures for Monitoring Scientific Misconduct," Nature 337 (16 February 1989): 588.

27. Idem, "Changes in Misconduct Investigation Planned," Nature 338 (16 March 1989): 189.

28. William Booth, "A Clash of Cultures at Meeting on Misconduct," Science 243 (3 February 1989): 598.

29. Gregory Byrne, "Fraud and the 'Glare of the TV Camera,'" Science 244 (2 June 1989): 1038.

30. Ibid.

31. Ibid.

32. Eli Ginzberg, "Political Economy of Public Health," in Public Health and Preventive Medicine, 11th ed., edited by John M. Last (New York: Appleton-Century-Crofts, 1980), pp.1846-54.

33. Ibid., p.1851.

34. Donald J. Philippon (Assistant Deputy Minister, Hospital Services Division) to Gerry Hiebert (President, Misericordia Hospital) 12 January 1989, Appendix C to this Thesis.

35. William Steinberg, "Extracorporeal Shockwave Lithotripsy: Human Resource, Supplies Budget and Associated Impact Areas," Study carried out by Misericordia Hospital task force, Edmonton, November 1988.

36. Lawrence C. Wiser, "A Time for Reflection: a Prospective Cost-Effectiveness Study of Lithotripsy in Northern Alberta," a paper written in partial fulfillment of the requirements for Health Services Administration 571, a postgraduate class in health care economics at the University of Alberta, Jan. - April 1989.

37. Section 32 of the Medical Devices Regulations defines "new device as "a device listed in the table to this Part (Part V)." The "table to this part," contains: 1) prolonged wear contact lens, 2) menstrual tampons, and 3) any device designed to be implanted into the tissues or body cavities of a person for 30 days or more. Canada, Health Protection Branch, Guide to the Preparation of a Submission to Part V of the Medical Devices Regulations (Ottawa: Minister of National Health and Welfare, 1984), p.3.

38. P. C. Milner et al., "Lithotripsy Versus Percutaneous Nephrolithotomy for Renal Calculi," British Medical Journal 297 (10 September 1988): 685.

39. Thomas C. Chalmers, "Randomization of the First Patient," Medical Clinics of North America 59 No. 4 (July 1975): 1035-38.

40. Canada, Health Protection Branch, Drugs Directorate Guidelines: Preparation of New Drug Submissions (Ottawa: Minister of National Health and Welfare, 1989), p.14. (unpublished.)

41. Calvin R. Stiller, "High-tech Medicine and the Control of Health Care Costs," Canadian Medical Association Journal 140 (15 April 1989): 905-08.

42. John E. F. Hastings and Eugene Vayda, "Health Services Organization and Delivery: Promise and Reality," in Medicine at Maturity, edited by Robert G. Evans and Greg L. Stoddart (Calgary: The University of Calgary Press, 1986), pp.337-38.

43. Charlotte Gray, "Health Care: Governments Use Right Code Words, but Cupboards are Bare," Canadian Medical Association Journal 140 (15 June 1989): 1493-94.

44. Ibid., p.1493.

45. Michael Rachlis and Carol Kushner, Second Opinion (Toronto: Collins Publishers, 1989), p.294.

46. Canada Health Act, R.S.C. 1985, c.C-6, s.3.

47. Lloyd F. Detwiller, "Canada's Thirty Years of Health Care Through Government: Where to From Here?" Inquiry 16 (Summer 1979): 101-07. The statute in force in Canada at the time of this publication by Detwiller (and the statute he is referring to), was the Medical Care Act, S.C. 1966-67, c.64. This statute was supplanted by the Canada Health Act which, if anything, is more forceful in its statement of purpose. Section 3 of the Canada Health Act (cited in the preceeding reference, 56 above) states:

> "It is hereby declared that the primary objective of Canadian health care policy is to protect, promote and restore the physical and mental well-being of residents of Canada and to facilitate reasonable access to health services without financial or other barriers."

48. Garrett Hardin, "The Tragedy of the Commons," Science 162 (13 December 1968): 1243-48.

49. Ibid., p.1244.

50. Howard H. Hiatt, "Protecting the Medical Commons: Who is Responsible?" The New England Journal of Medicine 293 (31 July 1975): 235-41.

51. Ibid., p.235.

52. Ibid.

53. Lewis Thomas, "Notes of a Biology-watcher: the Technology of Medicine," The New England Journal of Medicine 285 (9 December 1971): 1366-68.

54. Ibid., p.1367.

55. Ibid., p.1368.

56. Ibid.

57. Emil Thomas Kaiser and Susan Clark Brock, "Protein Inhibitors of Crystal Growth," The Journal of Urology 141 No. 3, Part 2 (March 1989): 750-52.

58. Mort Urivetsky, Jerry Weinberg and Arthur D. Smith, "Calcium Absorption and Excretion in Renal Stone Disease," The Journal of Urology 141 No. 4, Part 2 (April 1989): 208A, abstract 154.

59. Gordon Guyatt et al., "Guidelines for Health Technology Assessment: Therapeutic Technologies," in Health Care Technology: Effectiveness, Efficiency and Public Policy, edited by David Feeny, Gordon Guyatt and Peter Tugwell (Montreal: The Institute for Research on Public Policy, 1986), pp.57-77.

60. Op. cit. 50 above, p.240.

61. Celsus, quoted in W. I. B. Beveridge, The Art of Scientific Investigation (New York: W. W. Norton and Co., 1957), p.137.

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APPENDICES

APPENDIX A

LETTERS OF INQUIRY SENT

#74, 5215 - 110th Street,
Edmonton, Alberta. T6H 3K1

February 24, 1989

The Honourable P. Beatty,
Minister of Health and Welfare,
Brooke Claxton Building,
Tunney's Pasture,
Ottawa, Ontario.
K1A 0K9

Dear Minister:

I am a graduate student at the University of Alberta in Edmonton. I am in the last year of study leading to the degree of "Masters of Health Services Administration" (M.H.S.A.).

The topic of my masters Thesis is: "The way in which medical technology is diffused and implemented within the Canadian health care system", with special emphasis on overall cost and cost efficiency. I am especially interested in the new method of treating kidney stones by extracorporeal shock wave lithotripsy (ESWL). It is critical to my research to determine the method(s) used in Canada to assess, approve, ratify and implement new medical technologies as they appear on the scene; the lithotripter being a splendid example. What measures have been taken by the Government of Canada to assure that any new medical technology(ies) (i.e., the lithotripter in this example) is(are):

1) efficacious?
2) efficient?
3) safe?

Is the Government of Canada aware of any randomized clinical trials that have been completed in Canada or elsewhere involving the lithotripter? I have been unable to find any such studies prior to the implementation of ESWL in Canada or elsewhere.

I will thank you in advance for your cooperation in this matter. May I look forward to a reasonably prompt written response (within a month) to this inquiry so that my research may proceed to completion. Thank you for your attention to this matter. I remain,

Yours truly,

Lawrence C. Wiser

LCW/vl

#74, 5215 - 110th Street,
Edmonton, Alberta. T6H 3K1
CANADA.

February 24, 1989.

Donald Goldstone, M.D.,
Acting Director,
Office of Health Technology Assessment,
Rm. 18A-27,
5600 Fishers Lane,
Rockville, Md. 20857
U. S. A.

Dear Dr. Goldstone:

I am presently a graduate student at the University of Alberta in Edmonton, Alberta, Canada. I am in the last year of study leading to the degree of "Masters of Health Services Administration" (M.H.S.A.).

The topic of my masters Thesis is: "The way in which medical technology is diffused and implemented within the Canadian health care system", with special emphasis on overall cost and cost efficiency. I am especially interested in the new method of treatment for kidney stones which is extracorporeal shock wave lithotripsy (ESWL). It is critical to my research to determine the method(s) used to assess, approve, ratify and implement new medical technologies as they appear on the scene; ESWL being a splendid example. What measures have been taken by your office and the Government of the United States to assure that any new medical technology(ies) (i.e., ESWL in this case) is(are):

1) efficacious?
2) efficient?
3) safe?

Is your department aware of any randomized clinical trials that have been completed in the U.S. or elsewhere involving ESWL? I have been unable to find any such studies prior to the implementation of ESWL in Canada or the United States. I have in my possession a booklet from the U.S. Department of Health and Human Services, released in 1985 and entitled "Extracorporeal Shock Wave Lithotripsy (ESWL) Procedures for the Treatment of Kidney Stones: Number 1." Have there been any further studies done by your department dealing with this treatment specifically (I am only interested in the use of ESWL to treat kidney stones as opposed to gallstones).

Continued ...

I will thank you in advance for your cooperation in this matter. May I look forward to a reasonably prompt written response (within one month, if possible) from you to this inquiry and information (or references) regarding further ongoing assessments being carried out in this regard.

Thank you for your attention to this matter. I am

Yours truly,

Lawrence C. Wiser, M.D.

LCW/vl

#74, 5215 - 110 Street,
Edmonton, Alberta.
CANADA T6H 3K1

March 3, 1989.

Dr. James E. Lingeman,
Suite 655,
1801 North Senate Boulevard,
Indianapolis, Indiana. 46202
U. S. A.

Dear Dr. Lingeman:

I am presently a graduate student at the University of Alberta in Edmonton, Alberta, Canada. I am in the last year of study leading to the degree of "Masters of Health Services Administration" (M.H.S.A.).

The topic of my Masters Thesis is: "The way in which medical technology is diffused and implemented within the Canadian health care system" with special emphasis on overall cost and cost efficiency. I am especially interested in the new method of treatment for kidney stones which is extracorporeal shock wave lithotripsy (ESWL). It is critical to my research to determine the method(s) used to assess, approve, ratify and implement new medical technologies as they appear on the scene; ESWL being a splendid example. I have performed an exhaustive literature review (your name being very prominent among the authors who write about ESWL) and have yet to find any evidence of a randomized clinical trial to establish the value of ESWL by the U.S. Federal Drug Administration (U.S.F.D.A.) either before, during or after implementation of this technology. Are you aware of any such study that has been done or is currently being done? How has it been proven that ESWL is:

1) efficacious?
2) efficient?
3) safe?

Of particular interest to myself has been what I perceive as a shifting of your opinion and that of your group regarding the safety of ESWL regarding future kidney functioning. I have before me as I write the paper you and your colleagues wrote for the August (1988) edition of Urologic Clinics of North America, which I feel is just an excellent article. This work of yours (as I know you are aware) agrees with much of the work regarding ESWL that has been coming out of the University of Florida since 1985.

I (speaking as a physician), find myself somewhat leery of the rapid diffusion of this technology (i.e., ESWL) without what appears to be sufficient evaluation of the three factors previously mentioned, the most important of which is safety!

I would be very much interested in your thoughts on this matter as background for my Thesis. If you would give a written response to this letter of inquiry within one month's time, it would help me immeasurably in finishing off my degree, and I would be most grateful. I look forward to your reply. I am,

Yours truly,

Lawrence C. Wiser, M.D.

LCW/vl

#74, 5215 - 110th Street,
Edmonton, Alberta. T6H 3K1

February 24, 1989.

Dr. L. H. LeRiche,
Registrar,
College of Physicians &
Surgeons of Alberta,
9901 - 108 Street,
Edmonton, Alberta.
T5K 1G9

Dear Dr. LeRiche:

I am a graduate student at the University of Alberta. I am in the last year of study leading to the degree of "Masters of Health Services Administration" (M.H.S.A.).

The topic of my masters Thesis is: "The way in which medical technology is diffused and implemented within the Canadian health care system", with special emphasis on overall cost and cost efficiency. I am especially interested in the two shock-wave lithotripters which the Province of Alberta is about to purchase or has already purchased. It is critical to my research to determine the method(s) used in Alberta to assess, approve, ratify and implement new medical technologies as they appear on the scene; the lithotripter being a splendid example. What measures have been taken or will be taken by the College to assure that any new medical technology(ies) (i.e., the lithotripter in this case) is(are):

1) efficacious?
2) efficient?
3) safe?

Is the College aware of any randomized clinical trials that have been completed in Canada or elsewhere involving the lithotripter? I have not been able to find any such studies in my research.

I will thank you in advance for your cooperation in this matter. May I look forward to a reasonably prompt written response (within one month) to this inquiry so that my research may proceed to completion. Thank you for your attention to this matter, I remain

Yours truly,

Lawrence C. Wiser, M.D.

LCW/vl

#74, 5215 - 110th Street,
Edmonton, Alberta. T6H 3K1

February 24, 1989.

5

The Honourable Nancy Betkowski,
Minister of Health,
Rm. 130,
Legislature Building,
Edmonton, Alberta.
T5K 2B6

Dear Minister:

I am a graduate student at the University of Alberta. I am in the last year of study leading to the degree of "Masters of Health Services Administration" (M.H.S.A.).

The topic of my masters Thesis is: "The way in which medical technology is diffused and implemented within the Canadian health care system", with special emphasis on overall cost and cost efficiency. I am especially interested in the two shock-wave lithotripters which the Province of Alberta is about to purchase, or has already purchased. It is critical to my research to determine the method(s) used by the Province to assess, approve, ratify and implement new medical technologies as they appear on the scene; the lithotripter being a splendid example. What measures have been taken by the government of Alberta to assure that any new medical technology(ies) (i.e., the lithotripter in this case) is(are):

1) efficacious?
2) efficient?
3) safe?

Is the government of Alberta aware of any randomized clinical trials that have been completed in Canada or elsewhere involving the lithotripter? I have not been able to find any such studies in my research.

I will thank you in advance for your cooperation in this matter. May I look forward to a reasonably prompt response (within a month) in written form to this inquiry so that my research may proceed to completion. Thank you for your attention to this matter. I remain,

Yours truly,

Lawrence C. Wiser

LCW/vl

#74, 5215 - 110 Street
Edmonton, Alberta
T6H 3K1

April 6, 1989

Mr. G. Ward
Alberta Health
11010 - 101 Street
Edmonton, Alberta
T5J 2P4

Dear Mr. Ward:

Enclosed please find a copy of my letter to the Minister of Health of the Province of Alberta. A letter very much similar to that one was also sent to the Federal Minister of National Health and Welfare. I am enclosing a copy of his reply to my inquiry for your perusal.

I am trying to ascertain who in the health care delivery system (which person, office or branch of government) has the authority to approve a new medical "technology", thus releasing it into the public domain. The Federal Minister speaks of "label claims" which are "submitted by a manufacturer" (presumably to the federal government) to ensure that the device being sold is "safe and efficacious." But how does the new device (technology) become implemented for use by the public in Alberta? What ensures the safety of this new device? Do you get a look at this "label claim" which is said to be "proprietary"? Where does this label claim go? Are there any guidelines for its preparation and if so where can a copy of these guidelines be secured?

The preceding discussion of course refers to the advent of lithotripsy in Alberta (with which I know you are intimately acquainted) which provides a splendid example of this whole problem.

I thank you for taking the time and trouble to meet with me and if possible, would like to request a written response to these concerns. It is my hope that the project with which you have been involved in the last year proceeds smoothly.

Yours truly,

Lawrence C. Wiser

Enclosure

#74, 5215 - 110th Street,
Edmonton, Alberta. T6H 3K1

April 24, 1989.

Mr. K. Hutcheon,
Health Protection Branch,
3155 Willington Green,
Burnaby, B.C.
V5G 4P2

Dear Mr. Hutcheon:

Further to our telephone conversation of April 7 (which was extremely useful) please find copies of the letters we discussed. The first letter (dated February 24) is from me and poses several questions to Mr. Beatty (the federal Minister of National Health and Welfare). I think this letter is self explanatory, but as I mentioned on the phone, I am at this time becoming more concerned with the safety of this new lithotriptor device. As you can see in his reply, the Minister did not really address this issue and speaks of "label claims".

On the phone you mentioned "pre-market review" and "notice of compliance". I believe that you also mentioned that one, or both of these conditions did not apply in the case of the lithotriptor. I still find these distinctions in policy somewhat "fuzzy" in my own mind and hence this letter to you.

Please feel free to discuss at any length the present policy in place and used by the Government of Canada in deciding how a device such as the lithotriptor (or any new "hard" technology) is evaluated so as to ensure the safety of the public prior to and during the marketing and dissemination of the technology (product) since you seem to be the only one I have spoken to who understands it. Please feel free to send along any copies of policies, rules, regulations, etc. that you may have access to. I would be most appreciative if you could complete this task as briskly as possible. I am running somewhat of a time deadline with my research.

It was a pleasure talking to you and I look forward to your reply.

Yours truly,

Lawrence C. Wiser, M.D.

LCW/vl
Enc.

#74, 5215 - 110th Street,
Edmonton, Alberta. T6H 3K1

April 24, 1989.

Dr. Latourneau,
Bureau of Radiation and Medical Devices,
775 Brookfield Road,
Confederation Heights,
Ottawa, Ontario.
K1A 1C2

Dear Dr. Latourneau:

I am enclosing with this letter copies of two letters which have preceded it. You will note that I contacted Mr. Beatty on February 24, 1989 and I think that letter is self explanatory. I am enclosing a copy of his reply to that letter, dated March 29.

As my research into the diffusion of lithotripsy services in Canada progresses, I find the question of the safety of this technology coming forward more and more. I understand that it is your department which is responsible for ensuring that any new medical device being marketed in Canada (the lithotriptor being a prime example) is "safe" and "efficacious".

It is my hope that you can provide me with information regarding any:

1) policies
2) procedures
3) rules

in place at this time to ensure safety and efficiacy of extracorporeal shock wave lithotripsy or any new medical device that should appear for marketing. I invite you to send copies of any rules or guidelines that you follow.

In closing, I would point out that the Minister (Mr. Beatty) speaks of "label claims" which are "proprietary". Does your department get a look at these label claims? What is in them? What are the guidelines for their creation?

I thank you for your time and effort in responding to my inquiries. May I look forward to a reasonably prompt response from you as I am running out of time on this research project.

Yours truly,

Lawrence C. Wiser, M.D.

LCW/vl
Enc.

APPENDIX B

LETTERS RECEIVED

Minister of National Health
and Welfare

CANADA

Ministre de la Santé nationale
et du Bien-être social

177

Ottawa, K1A 0K9

29 III 1989

Mr. Lawrence C. Wiser
#74, 5215 - 110th Street
Edmonton, Alberta
T6H 3K1

Dear Mr. Wiser:

Thank you for your letter of February 24, 1989, pertaining to the diffusion and implementation of medical technology within the Canadian health care system.

The Department of National Health and Welfare does not approve medical devices or the associated technologies. Rather, it is the manufacturer's responsibility to ensure that medical devices which he sells are safe and efficacious when used as directed.

Information submitted by a manufacturer to support his label claims is considered to be proprietary, and not available for dissemination to the public. Hence if you would like details of clinical trials, I suggest that you consult a medical school library.

Good luck with your studies.

Sincerely,

Perrin Beatty

Perrin Beatty

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Rockville MD 20857

National Center for Health Services Research
and Health Care Technology Assessment

Room 18A-27
5600 Fishers Lane

APR -4 1989

Lawrence C. Wiser, M.D.
#74, 5215 - 110th Street
Edmonton, Alberta. T6H 3K1
CANADA

Dear Dr. Wiser:

This is in response to your letter of February 24 regarding technology assessment and in particular how it pertains to shock wave lithotripsy. As you have correctly stated our office assessed shock wave lithotripsy in 1985. Enclosed is a program profile to help explain our technology assessment program. We are currently revising our medical coverage process procedures manual. The revised manual will be made available as soon as it is completed.

To date, the Food and Drug Administration (FDA) has given three companies permission to market their lithotripsy devices. The Summary of Safety and Effectiveness Data Reports for those devices have been provided for your use.

A National Institutes of Health Consensus Development Conference on Prevention and Treatment of Kidney Stones was held in March 1988. Enclosed is the information from that conference. According to the NIH there has been little additional information since the conference.

I hope the information provided is helpful to you. Best of luck with your studies.

Donald E. Goldstone, M.D.
Acting Director
Office of Health Technology Assessment

Enclosures

Methodist
Hospital OF INDIANA, INC.

INSTITUTE FOR KIDNEY STONE DISEASE
1801 North Senate Boulevard, Suite 690
P.O. Box 1367
Indianapolis, IN 46206
(317) 92-STONE

June 6, 1989

Lawrence C. Wiser, M.D.
#74, 5215 - 110 Street.
Edmonton, Alberta.
CANADA T6H 3K1

Dear Dr. Wiser:

Thank you for your recent letter and call regarding the diffusion of ESWL technology. The diffusion of any medical technology is affected by many factors other than pure science. Certainly the noninvasive nature of ESWL has been a major driving force in its rapid adoption and acceptance by patients and physicians throughout the world. Nonetheless, the most important issue needing to be addressed regarding ESWL remains not who can be treated, but rather who should be treated with this exciting new technology.

Clearly, not all patients are good candidates for ESWL. Ideal candidates would seem to be patients with limited stone burden and otherwise normal renal collecting systems. On the other hand, patients with substantial stone burden, lower pole calyceal stones between 1 and 2 cm in diameter, renal calculi associated with calyceal diverticula, and horseshoe kidneys are less clearly benefited by ESWL. Percutaneous nephrostolithotomy has been demonstrated to be very efficacious in these more complex stone problems. For this reason, prospective randomized clinical trials of ESWL versus percutaneous nephrostolithotomy are probably the best way to examine the relative efficacy, cost, and morbidity of these two forms of treatment for nephrolithiasis.

Sincerely,

James E. Lingeman, M.D.

JEL/lc

FAX (317) 924-7791

College of Physicians and Surgeons

PROVINCE OF ALBERTA
Dr. L. H. le RICHE
REGISTRAR

DIRECT ALL CORRESPONDENCE
TO THE REGISTRAR

9901 - 108 STREET
EDMONTON, ALBERTA
T5K 1G9

PHONE 423-4764
AREA CODE 403

May 17, 1989

Dr. Lawrence C. Wiser
74, 5215 - 110 Street
EDMONTON, Alberta
T6H 3K1

Dear Dr. Wiser:

I am in receipt of your letter of the 24th ultimo, but did not receive the one of February 24, 1989.

The Council of the College of Physicians and Surgeons does not investigate every new modality in medical technology unless there is a specific reason to do so. The Council relies on publications in reputable journals. Also, should the Council need to explore anything new in medicine, it will go the authorities on the subject.

The Council has not made a study into whether lithotripters are efficacious, efficient or safe.

Yours truly,

L.H. le Riche, M.B., Ch.B.
Registrar

LHl/mea

Alberta
HEALTH

P.O. Box 2222, 11010 - 101 Street, Edmonton, Alberta, Canada T5J 2P4 403/427-6085

March 15, 1989

Dr. Lawrence C. Wiser
#74, 5215 - 110 Street
Edmonton, Alberta
T6H 3K1

Dear Dr. Wiser:

Thank you for your letter dated February 24, 1989, addressed to the Minister of Health, requesting information on the diffusion and implementation of medical technologies in Canada, and specifically the technology of lithotripsy.

I suggest that the most effective way to gather this information is for you to meet with staff of the Department. If you could telephone Mr. Gordon Ward at 427-6076 he will assist you in this regard.

I wish you every success in the completion of your masters thesis.

Yours truly,

Donald J. Philippon
Assistant Deputy Minister
Hospital Services Division

Health and Welfare Canada
Santé et Bien-être social Canada

Health Protection Branch
Direction générale de la protection de la santé

Drug & Environmental Health
Inspection Division
3155 Willingdon Green
Burnaby, B.C.
V5G 4P2

May 10, 1989

File: 9448-1-1

Dr. Lawrence C. Wiser
#74, 5215-110th Street
Edmonton, Alberta
T6H 3K1

Dear Dr. Wiser:

Further to your letter of April 24, 1989, I enclose for your information the following:

1. The Medical Devices Regulations including excerpts from the Food and Drugs Act pertaining to devices.
2. Publication 85-EHD-118 Medical Devices - Canadian Regulatory Requirements - Questions and Answers
3. Guide to the Preparation of a Submission Pursuant to Part V of the Medical Devices Regulations.

A Notice of Compliance (pre-market review) is required for only those devices listed in the table to Part V of the Medical Devices Regulations. For all other devices there is no mechanisms under the Food and Drug Act to formally approve or evaluate same prior to sale. The onus is on the manufacturer to ensure compliance with all requirements of the Medical Devices Regulations including Safety and Efficacy.

I trust the information provided will be of assistance to you.

Yours truly,

A.A. Hutcheon
Medical & Radiation
Emitting Devices Inspector

Canada

Health and Welfare Canada / Santé et Bien-être social Canada

Health Protection Branch / Direction générale de la protection de la santé

Bureau of Radiation and Medical Devices
775 Brookfield Road
OTTAWA, Ontario
K1A 1C1

May 3, 1989

Dr. Lawrence C. Wiser
#74, 5215 - 110th Street
EDMONTON, Alberta
T6H 3K1

Dear Dr. Wiser:

Your letter dated April 24, 1989 addressed to Dr. Létourneau concerning the safety and efficacy of new devices, and lithotriptors in particular, has been referred to me for reply.

Lithotriptors are not included in the definition of "new device", and are not subject to the requirements of Part V of the Medical Devices Regulations. Hence there is no premarket review of a manufacturer's claims relating to safety and efficacy.

Enclosed for your information please find copies of the Medical Devices Regulations, Guidelines for the Preparation of a Part V Submission and an explanatory booklet concerning Canadian regulatory requirements. The Table to Part V lists those devices which are considered to be "new devices".

Manufacturers' label claims are not proprietary. Rather, it is the information which is submitted by a manufacturer to support the label claims which must be treated as proprietary. There are no specific guidelines for label claims other than what is stated in the Food and Drugs Act and the Medical Devices Regulations.

. . ./2

Canada

If you would like specific clinical information on lithotripsy, the Bureau's Clinical Advisory Divison may be able to assist you. I have forwarded a copy of your letter to Dr. S. Mohanna, Chief, Clinical Advisory Division, Bureau of Radiation and Medical Devices, Environmental Health Centre, Tunney's Pasture, Ottawa, K1A 0L2.

Yours sincerely,

WJWelsh

W.J. Welsh
A/Chief,
Pre-Market Division

Telephone: (613) 954-6701

WJW:fc

c.c.: Dr. S. Mohanna

Alberta
HEALTH
P.O. Box 2222, 11010 - 101 Street, Edmonton, Alberta, Canada T5J 2P4 403/427-6085

June 19, 1989

Dr. Larry Wiser
#74, 5215 - 110 Street
Edmonton, Alberta
T6H 3K1

Dear Dr. Wiser:

The following information relates to the establishment of Extracorporeal Shock Wave Lithotripsy services in the province of Alberta. The units both in Calgary and Edmonton are considered a provincial resource.

The Government of Alberta announced on March 21, 1988, its approval to utilize lottery funds for the purchase of two Extracorporeal Shock Wave Lithotripters. One unit would be installed at the Holy Cross Hospital in Calgary and the other unit at the Misericordia Hospital in Edmonton. The chosen Extracorporeal Shock Wave Lithotripters have the capacity to treat both renal and biliary calculi.

The purchase of two Extracorporeal Shock Wave Lithotripters was consistent with a report submitted to Alberta Health in August, 1986. A Committee comprised of a group of experts in the fields of urology and radiology, and some hospital administrators were requested to prepare a report for the future utilization and deployment of lithotripsy units in the Province of Alberta.

An External Committee, whose members included representatives from the Alberta Health, the Misericordia Hospital and the Holy Cross Hospital, began meeting in early August, 1988 to plan for the implementation, utilization, monitoring and the development of an assessment process of the two Extracorporeal Shock Wave Lithotripters. The members of the Committee have worked extensively to develop provincial accessibility and referral protocols. As well they have been instrumental in designing a general assessment study which will capture some data relating to demographic, diagnostic, utilization, patient outcome, and comparative data on the various treatment modalities for renal calculi.

The two hospitals independently conducted a detailed equipment selection process, which was completed by the end of 1988. The Lithostar Plus manufactured by Siemens Electric

.../2

Limited was chosen from a total of nine companies who submitted bids. The selection process was a team effort involving the radiologists, urologists, gastroenterologists and general surgeons.

The lottery funds were released to the Misericordia and Holy Cross Hospitals at the end of January 1989. If renovations are completed on schedule the two units should be operational by June 1, 1989. This will allow patients to be treated with the latest state-of-the-art technology for urolithiasis. The multi-functional capabilities of the Lithostar Plus will make it possible to extend its range of services to include the treatment of biliary calculi.

I hope this information is useful and assists you in your endeavours.

Yours truly,

Gordon Ward
Assistant Director
Provincial Programs
and Capital Planning

GW:mc

APPENDIX C

OTHER LETTERS

FACSIMILE

December 22, 1988

Mr. G. Ward
Department of Health
P.O. Box 2222
11010 - 101 Street
Edmonton, Alberta
T6J 2P4

Dear Mr. Ward

As indicated in my letter of December 5, 1988 to you the review/selection committee has made a decision in favor of Siemens Electric Ltd., for the Lithostar Plus Extracorporeal Shock Wave Lithotripter with the gallbladder attachment.

Final cost analysis is as follows:

1.	Lithotripter Equipment Cost	$1,819,155.00
2.	Additional Accessories	57,830.00
3.	Renovations (see Appendix B)	225,000.00

At this time the Misericordia Hospital requests final approval and funding from the Department of Health.

I would like to take this opportunity to wish you a very Merry Christmas and best wishes for the New Year.

Yours sincerely,

Dr. D. C. Perry
Vice President, Medical

DCP/bg

Alberta
HEALTH
P.O. Box 2222, 11010 - 101 Street, Edmonton, Alberta, Canada T5J 2P4 403/427-8086

File No. H041-08

Office of the President
RECEIVED
JAN 17 1989
MISERICORDIA HOSPITAL

January 12, 1989

Mr. G Hiebert
President
Misericordia Hospital
16940 - 87 Avenue
Edmonton, Alberta
T5R 4H5

Dear Mr. Hiebert:

Re: Misericordia Hospital

I am pleased to inform you that the Department of Health has requested Lottery revenue to issue a cheque in the name of the Misericordia Hospital for the amount of $1,981,655. This will enable you to proceed with the acquisition of a lithotripter unit from Siemens Electric Ltd. and accessories from other vendors. A breakdown of the disposition of the funds is attached to this letter.

I wish to commend those members of the various committees involved in this important project. It will result in a service, recognized as a provincial resource, with universal accessibility to all patients and physicians in Northern Alberta.

Yours truly,

Donald J. Philippon
Assistant Deputy Minister
Hospital Services Division

DJP:nd/b

Attachment